

Cardiology

A Practical

Handbook

David Laflamme

Foreword by Dr Paul Dorian



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roche



CRC Press
Taylor & Francis Group

Cardiology

A Practical Handbook



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There has been a near exponential increase in the amount of information available on the pathophysiology and management of heart diseases over the past decades. Meanwhile, our understanding of the underlying pathology and physiology has deepened and broadened with new methodologies to monitor cardiac structure and function. These developments have led to an overwhelming amount of information available to students, trainees, and physicians on all aspects of cardiac disease. What is in short supply is a comprehensive yet concise and clear description of the important cardiac conditions and disorders, an approach to their management, and an easily consulted and well indexed summary to be used at the bedside or in the clinic.

The Cardiology Handbook fills an extremely important, not well occupied niche in providing junior and senior practitioners alike with a brief yet detailed summary of “what you need to know” about virtually all important cardiovascular conditions.

This handbook does not aim to be a comprehensive review of all of the evidence pertaining to pathophysiology, investigation, and treatment of cardiovascular disorders. It does however wonderfully clearly get “straight to the point” and I think will be a frequently used and extremely effective resource for a brief “look up” in the clinic, in the emergency room, and on the wards.

I anticipate this handbook will be a treasured resource for senior medical students, trainees in internal medicine, emergency medicine, anesthesia, and other specialties where cardiovascular disorders are commonly seen. The effective use of figures and tables makes this appealing both visually and cognitively, and for those unfamiliar with the complex and varied terrain of cardiovascular medicine, will prove an outstanding trail map to allow successful navigation of unfamiliar terrain. In an era where there is often “too much information”, this handbook provides just the right amount.

Sincerely,

A handwritten signature in black ink, reading "Paul Dorian". The signature is fluid and cursive, with the first name "Paul" and last name "Dorian" clearly distinguishable.

Paul Dorian, MD, FRCPC, FHRS
Dexter H.C. Man Chair in Cardiology
Director Division of Cardiology, University of Toronto
Past President, Canadian Heart Rhythm Society



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*To my parents, Diane and Marcel,
for their constant support,
and to Anne-Sophie, for
her extraordinary patience.*

Cardiology is a fascinating medical specialty. This vast discipline combines various fields of expertise, including research, prevention, clinical evaluation, diagnostic examinations, therapeutic management, invasive interventions and rehabilitation.

As a result of the spectacular progress over the last two decades, cardiology now comprises sophisticated and advanced diagnostic and therapeutic tools (validated by evidence-based medicine) allowing cardiologists to more effectively manage their patients, who have greatly benefited in terms of survival and/or quality of life.

In relation to such an effervescent and increasingly complex discipline, physicians who have the privilege to practice cardiology must have access to resources that enable them to acquire, update, refine and organize their knowledge.

The purpose of this book is to provide a concise overview of modern cardiology. More than 10,000 pages of references have been condensed and organized into less than 350 pages. This pocket book provides practising clinicians with specific and accurate information on a particular subject. It is also designed to allow students, interns and all other personnel working in the field of cardiology to acquire and organize their valuable knowledge.

The design of this cardiology handbook was a captivating but colossal task. The information presented in this book is derived from numerous valid and up-to-date sources and has been verified by various reviewers, experts in their respective fields. The various recommendations are also derived from American, European or Canadian learned society evidence-based guidelines.

I sincerely hope that this book will inspire or maintain your passion for cardiology and I wish you an enjoyable read.

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February 2016

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Legal statement

Every physician is responsible for his or her acts. Although the recommendations and management presented in this book are based on valid, reliable and up-to-date references at the time of writing, the author and publisher decline all responsibility and remind the reader that every physician must practice medicine according to current medical and scientific guidelines, taking into account his or her own capacities and limitations, and, if necessary, seeking advice from more experienced specialists.





Cardiac diagnostic assessment

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1.1/ CARDIAC PHYSICAL EXAMINATION

EXAMINATION OF THE PATIENT

GENERAL INSPECTION: Diaphoresis; Signs of hypoperfusion; Cachexia; Mitral facies; Cheyne-Stokes breathing

CUTANEOUS INSPECTION: Cyanosis (central vs peripheral); Pallor; Telangiectasias (Osler-Weber-Rendu; scleroderma); Tanned skin (hemochromatosis); Jaundice (liver disease); Ecchymoses (coagulopathy); Petechiae (thrombocytopenia); Purpura (vasculitis; endocarditis); characteristic axillary skin fold (pseudoxanthoma elasticum); Lentiginosis (LEOPARD; Carney); Lupus pernio - erythema nodosum (sarcoidosis); blue sclera (osteogenesis imperfecta); nicotine stains (smoking)

- **Familial hypercholesterolemia:** Arcus senilis; pathognomonic tendinous xanthomas (extensor tendons; MCP; Achilles tendon); Xanthelasma
- **Familial hypertriglyceridemia (LPL deficiency):** Eruptive xanthomas; Lipemia retinalis
- **Dysbetalipoproteinemia:** Tuberous xanthomas (elbows; knees); Palmar xanthomas

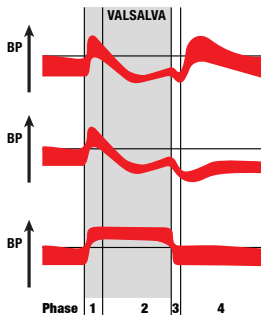
SIGNS OF ENDOCARDITIS: Roth's spots; Janeway lesions; Osler's nodes; splinter hemorrhages; mucosal petechiae

FUNDUSCOPY: hypertensive retinopathy (arteriovenous nicking; exudates; hemorrhages; cotton-wool spots; papilledema); diabetic retinopathy; endocarditis (Roth's spot); Hollenhorst plaque (cholesterol embolism); Lipemia retinalis

VITAL SIGNS

BLOOD PRESSURE: in both arms (\pm legs)

- **Large pulse pressure ($> 50\%$ of SBP):** Age - HTN; AR; Patent ductus arteriosus; Ruptured aneurysm of the sinus of Valsalva; Fever; Anemia; Hyperthyroidism; Pregnancy; AV fistula; Paget's disease
- **Narrow pulse pressure ($< 25\%$ of SBP):** Cardiac tamponade; Heart failure; Cardiogenic shock; Aortic stenosis
- **BP difference between the two arms > 10 mmHg:** Normal variant; PAD; Inflammatory vascular disease (Takayasu; giant cell arteritis); Supravalvular aortic stenosis; CoA; Aortic dissection
- **BP difference between the arms and legs > 20 mmHg:** Hill's sign (significant AR); CoA; severe PAD
- **Pulsus paradoxus:** \searrow SBP > 10 mmHg on inspiration
- **Orthostatic hypotension:** \searrow SBP > 20 mmHg or \searrow DBP > 10 mmHg during the first 3 minutes after standing up
- **Valsalva response**



NORMAL RESPONSE (SINUSOIDAL)

1. \uparrow BP (\uparrow intrathoracic pressure)
2. \downarrow venous return; \downarrow BP; \uparrow SVR; Reflex tachycardia
3. Release: \downarrow BP (brief)
4. Overshoot: \uparrow venous return; \uparrow BP; \downarrow SVR; Reflex bradycardia

NO OVERSHOOT (PHASE 4)

Systolic dysfunction

SQUARE WAVE

\uparrow filling pressure (little impact of \downarrow venous return)

OTHER VITAL SIGNS: Pulse; heart rate regularity; Respiratory rate; Oxygen saturation; Temperature; Weight; Height; Waist

> **Body surface area (m²) = 0.007184 x weight (kg) x height (cm)**

+

NECK

CAROTID PULSE

- > **Shape:** ▶▶ Hemodynamic assessment (arterial recording)
- > **Carotid sinus massage:** abnormal response if **asystole > 3 seconds (sinus arrest or AV block)** and/or **significant and symptomatic fall in SBP**

+

JUGULAR VEINS

- > **Jugular vein vs carotid artery:** Biphasic; Height modified by inspiration and position and hepatojugular reflux (HJR); Impalpable; Compressible
- > **Height:** distance between the sternal angle and the summit of venous pulsation; **normal < 3 cmH₂O**
 - **CVP (cmH₂O):** height above the sternal angle + 5 cmH₂O
 - **Normal CVP:** < 8 cmH₂O (< 6 mmHg)
 - **Conversion:** 1.36 cmH₂O = 1 mmHg
- > **Waves:** ▶▶ Hemodynamic assessment (atrial recording)

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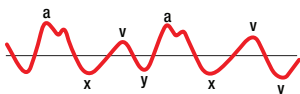
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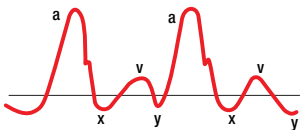
Normal pattern

a wave > v wave



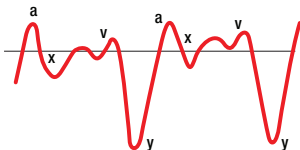
Tricuspid stenosis (or RVH)

Predominant a wave



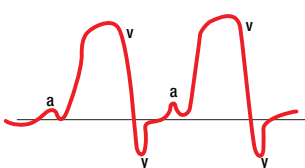
Constrictive pericarditis

Predominant y descent / W (or M) pattern



Tricuspid regurgitation

Predominant v wave



- > **Kussmaul's sign:** inspiratory increase (or absence of decrease) of CVP (constriction; RCM; RV infarction; pulmonary embolism; TS; RA tumor; right heart failure)
- > **Hepatjugular reflux (HJR):** Right upper quadrant (RUQ) compression (25 mmHg) x 15 seconds
 - **Abnormal response:** sustained \nearrow of CVP > 3 cm throughout compression (patient breathing normally); **reflects right heart failure and/or wedge pressure > 15 mmHg**

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01

Cardiac diagnostic assessment

PRECORDIUM

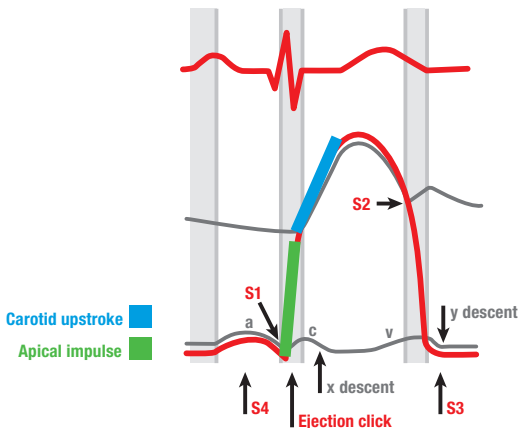
INSPECTION OF THE RIB CAGE: pectus excavatum; pectus carinatum; kyphoscoliosis; barrel chest; surgical scars; breathing; PPM / ICD

INSPECTION OF THE PRECORDIUM: position and dimensions of the apical impulse

PALPATION: patient in 30° supine position

- > **Apical impulse:** with the fingertips; left lateral supine position as required; **medial to the midclavicular line; 4th or 5th intercostal space; diameter < 2 cm** +
- **Apical pulsation:** corresponds to isovolumic contraction of the LV
- **Hyperdynamic apex:** increased amplitude of apical impulse but of normal duration; AR; patent ductus arteriosus; MR; VSD; hyperthyroidism; anemia; pregnancy
- **Sustained apical impulse:** the impulse persists during or after the carotid upstroke +
- **Enlarged apical impulse:** dilatation > 2 cm and/or shift downwards and to the left; associated with **LV volume overload** +
- **Palpable S3:** LV volume overload
- **Palpable S4:** noncompliant LV / ↑ end-diastolic pressure
- **Triple apical impulse:** HCM (early-systole; end-systole due to dynamic LVOT obstruction; S4)
- > **Ectopic pulsation:** LV aneurysm (mid-precordial or anterior axillary)
- > **Left parasternal heave:** associated with RVH
- > **Thrill:** palpate the 4 areas (palm of the hand at the level of the MCP joints)
- > **Pulsation in the 2nd right intercostal space:** ascending aortic aneurysm
- > **Pulsation in the 2nd left intercostal space:** PA dilatation

AUSCULTATION - SYSTOLIC HEART SOUNDS



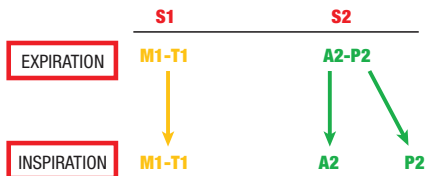
LOOK FOR: S1; Ejection click; Mid-systolic click; S2

S1: M₁-T₁ (interval: 20-30 ms); maximum at the apex; T1 mainly in the 5th left intercostal space; precedes the carotid upstroke

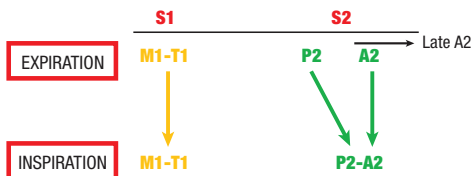
- > ↗ **Intensity of S1 ($S1 \geq S2$ in the 2nd left intercostal space)**: Rheumatic MS (early stage); Hyperdynamic state (↗ dP/dt); PR < 120 ms; ↗ flow through mitral valve (VSD; patent ductus arteriosus)
- > ↘ **Intensity of S1**: Calcified MS (↘ mobility); Systolic dysfunction; PR > 200 ms; acute AR
- > **Variable intensity of S1**: AF; AV dissociation; Tamponade
- > **Split S1 (split sound in the 5th left intercostal space)**: RBBB; ASD (delayed T1); ST (delayed T1); Ebstein's anomaly

S2: A2-P2; maximum in the 2nd left intercostal space

- > **Normal physiological splitting**: on inspiration; 2nd left intercostal space; interval: 20-60 ms



- > **Normal but narrow inspiratory splitting**: PHT (associated with ↗ P2)
- > **Increased splitting**: RBBB; severe MR (early A2); VSD (early A2); RVOT obstruction (late P2)
- > **Fixed splitting (A2-P2 variation < 20 msec)**: ASD; right heart failure (absence of variation of ejection volume according to RV preload)
- > **Paradoxical splitting**: LBBB; RV PPM; AS; HCM; LV systolic dysfunction; AR (prolonged ejection)



- > ↗ **intensity of A2**: HTN; CoA; Ascending aortic aneurysm; Transposition of the great arteries; supralvalvular AS
- > ↘ **intensity of A2**: Valvular AS; AR
- > ↗ **intensity of P2**: P2 > A2 in the 2nd left intercostal space or P2 heard at the apex or palpable P2; PHT; Supralvalvular RVOT obstruction
- > ↘ **intensity of P2**: Valvular PS; pulmonary regurgitation (except if secondary to PHT); Transposition of the great arteries
- > **Single S2**: ↘ A2 (AS) or ↘ P2 (PS); Transposition of the great arteries

VALVULAR EJECTION CLICK: coincides with carotid upstroke (120-140 ms after QRS);

high-pitched sound; diffuse radiation; best heard in lower left parasternal region; associated with bicuspid aortic valve (valve still pliable) or congenital PS (↘ click on inspiration; valve still pliable) +

- > **Vascular ejection click**: Aortic root dilatation; PA dilatation (idiopathic; post-stenotic; PHT)

MID-SYSTOLIC CLICK OF MVP: non-ejection click (after the carotid pulsation); high-pitched sound; earlier if the patient stands up; ± MR murmur

AUSCULTATION - DIASTOLIC HEART SOUNDS

LOOK FOR: S2; Opening snap; Pericardial knock; S3; Tumor plop; S4; Friction rub

MITRAL OPENING SNAP: High-pitched sound; stethoscope diaphragm at the apex; **A2-opening snap interval inversely proportional to the severity of MS** (40-120 ms after S2); interval decreases with tachycardia; ↘ intensity of opening snap when the valve is calcified

PERICARDIAL KNOCK: Constrictive pericarditis; early diastolic sound (at the end of the y descent); 100-120 ms after S2

S3: left lateral supine position; stethoscope bell at the apex; 140-160 ms after S2; during rapid ventricular filling (at the end of the y descent); associated with **ventricular volume overload** +

- > **Etiologies:** Dilated cardiomyopathy; heart failure; MR; AR; VSD; patent ductus arteriosus; diastolic dysfunction; young subjects in good health; normal pregnancy
- > **Right S3:** lower left parasternal region; ↗ on inspiration; TR; right heart failure; PHT

S4: left lateral supine position; stethoscope bell at the apex; occurs during atrial kick (after the P wave); associated with a **poorly compliant ventricle** and ↗ **filling pressure** +

- > **Etiologies:** HTN; AS; HCM; LVH; Ischemia; Acute AR; Acute MR; Age
- > **Right S4:** lower left parasternal region; ↗ on inspiration; RVOT obstruction; PHT

SUMMATION GALLOP: fusion of S3 and S4 during tachycardia

TUMOR PLOP: prolapse of the tumor through the AV valve; sound varies with position

PERICARDIAL FRICTION RUB: 1 or 2 or 3 components (rapid ventricular filling; atrial kick; ventricular systole); forced expiration while leaning forward; stethoscope diaphragm in left parasternal region

AUSCULTATION - MURMURS

IDENTIFY: Moment of the cycle; Configuration (crescendo; decrescendo; crescendo-decrescendo; plateau); Site; Radiation; Tone; Intensity; Modifiers (breathing; special maneuvers)

- > **1/6:** Very faint murmur (barely perceptible)
- > **2/6:** Faint murmur but heard immediately
- > **3/6:** Moderate murmur
- > **4/6:** Palpable thrill
- > **5/6:** Very loud; heard even when only part of the stethoscope is in contact with the chest
- > **6/6:** Heard even when the stethoscope is not in contact with the chest

BENIGN MURMUR: 1-2/6 in left parasternal region; Ejection murmur; S2 of normal intensity with normal physiological splitting; No other heart sounds or murmurs; No LVH (on examination or ECG); Murmur not increased by Valsalva maneuver or standing

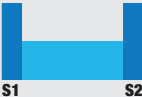





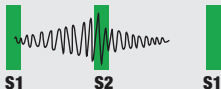
INDICATIONS FOR TTE: Diastolic or continuous or holosystolic or end-systolic or early systolic murmur or associated with ejection click or ≥ 3/6 with mid-systolic peak or radiating to the neck or back or signs or suspicion of MR, MVP, HCM or VSD on dynamic auscultation

SYSTOLIC MURMUR

**Mid-systolic
(often diamond-shaped)**



- Benign
- Ejection murmur: High output state (pregnancy; hyperthyroidism; anemia; AV fistula; AR; PR; ASD)
- Aortic stenosis (supra-avalvular; valvular; subvalvular)
- Aortic sclerosis
- HCM
- PS (supra-avalvular; valvular; subvalvular)
- CoA
- Functional / ischemic MR

Holosystolic  <p>S1 S2</p>	<ul style="list-style-type: none"> • MR • TR • VSD (restrictive)
Early systolic  <p>S1 S2</p>	<ul style="list-style-type: none"> • Acute MR • Primary TR (without PHT) • VSD: small muscular VSD or large VSD with significant PHT
End-systolic  <p>S1 S2</p>	<ul style="list-style-type: none"> • MVP • Functional / ischemic MR (↗ on exercise) • Tricuspid valve prolapse
DIASTOLIC MURMUR (ALWAYS INVESTIGATE)	
Early diastolic  <p>S2 S1</p>	<ul style="list-style-type: none"> • AR • Graham-Steell: PR secondary to PHT (decrecendo; high-pitched; signs of associated PHT) • PR without PHT (faint murmur)
Mid-diastolic  <p>S2 S1</p>	<ul style="list-style-type: none"> • MS • TS • Austin-Flint (absence of opening snap) • Myxoma • ↗ diastolic flow through AV valve (MR; TR; VSD; patent ductus arteriosus; ASD; abnormal pulmonary venous return) • Carey Coombs murmur (mitral valvulitis during acute rheumatic fever)
End-diastolic  <p>S2 S1</p>	<ul style="list-style-type: none"> • MS (presystolic accentuation) • TS • Austin-Flint • Myxoma • Rydand's murmur: diastolic mitral regurgitation in a context of complete AV block
CONTINUOUS MURMUR (OFTEN PATHOLOGICAL)	
Starts at systole and continues uninterrupted during diastole  <p>S1 S2 S1</p>	<ul style="list-style-type: none"> • Patent ductus arteriosus (Gibson's murmur; machinery murmur) • Aortopulmonary window • Coronary arteriovenous fistula • Ruptured aneurysm of the sinus of Valsalva • Neck venous hum • Mammary murmur of pregnancy • Stenosis of peripheral branch of pulmonary artery • Lutembacher's syndrome: MS + ASD • CoA / Intercoastal collateral vessels • Pulmonary or systemic AV fistula • Bronchial collateral vessels

DYNAMIC AUSCULTATION

MANEUVERS	AS	HCM	MVP	MR	OTHER
Valsalva (↘ preload)	↘	↗	↗ duration of murmur	↘	↘ AR
Standing up (↘ preload)	↘	↗	↗ duration of murmur	↘	
Squatting or leg raising (↗ preload)	unchanged or ↗	↘	↘ duration of murmur	↗	↗ AR - ↗ VSD
Hand grip (↗ afterload)	unchanged or ↘	↘	↘ duration of murmur	↗	↗ AR - ↗ VSD ↗ MS (↗ HR)
Amyl nitrate (↘ afterload)	↗	↗	↗ duration of murmur	↘	↗ MS (↗ HR) ↘ AR - ↘ VSD ↘ Austin Flint
Post-PVC (↗ contractility)	↗	↗	↘ duration of murmur (↗ LV volume)	un- changed	

INSPIRATION: louder right heart sounds/murmurs (except for pulmonary valve ejection click);
↗ splitting of S2

PHYSICAL EXAMINATION - OTHER EXAMINATIONS

LUNGS: crackles; effusion; wheezing; pleural friction rub

ABDOMEN: Liver (pulsation); Ascites; Splenomegaly; Aorta; Murmurs

LOOK FOR PRESACRAL EDEMA

UPPER LIMBS: clubbing; arachnodactyly; signs of endocarditis; nicotine stains; sclerodactyly; pulse in both arms

LOWER LIMBS: murmurs; lower limb edema; pulse in both legs; capillary refill; discoloration; ulcer; coldness; atrophic changes; hair loss

➤ **Radiofemoral delay:** CoA

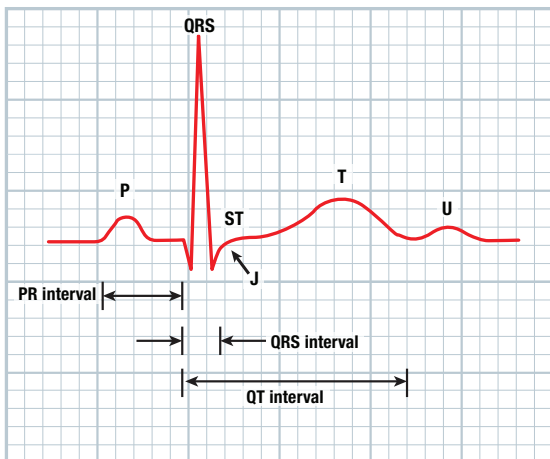
➤ **Pulse:** 0 = absent; 1 = decreased; 2 = normal; 3 = bounding

BRIEF NEUROLOGICAL EXAMINATION

1.2/ ELECTROCARDIOGRAM (ECG)

SYSTEMATIC APPROACH

- HEART RATE:** 1500 / number of small squares between 2 QRS or 300-150-100-75-60-50-43-38
- RHYTHM** (▶▶ Chapter 6 - Arrhythmias)
- P WAVE:** morphology
- AV CONDUCTION**
- QRS:** frontal axis; intraventricular conduction; precordial QRS transition; voltage / chamber hypertrophy
- REPOLARIZATION:** ST segment - T wave - QT interval - U wave
- MYOCARDIAL INFARCTION / Q WAVE**



NORMAL VALUES	
Calibration	<ul style="list-style-type: none"> • Vertical: 10 mm = 1 mV • Horizontal: 1 mm = 40 msec
P wave duration and amplitude	< 120 ms and < 2.5 mm in amplitude
P wave axis	60° (positive I-II-aVL-aVF; negative aVR) Normal axis: 0-90°
PR interval	120-200 ms
QRS duration	≤ 110 ms
QRS axis	-30° to +90°
Precordial QRS transition	R = S in V3 or V4
QRS amplitude	<ul style="list-style-type: none"> • Limbs: > 5 mm • Precordial: > 10 mm
J Point / ST segment	Elevation <ul style="list-style-type: none"> • V2-V3: < 2 mm (men > 40 years); < 2.5 mm (men < 40 years); < 1.5 mm (women) • Other leads: < 1 mm Depression: < 0.5 mm
T wave	<ul style="list-style-type: none"> • Positive: I-II-V3-V4-V5-V6 • Negative: aVR • Variable: aVL-III-V1-V2 • Maximum amplitude V2: < 14 mm (men) and 10 mm (women)
QTc	<ul style="list-style-type: none"> • Men: < 450 ms • Women: < 460 ms

TECHNICAL CONSIDERATIONS

ARM LEAD REVERSAL: P and QRS and T wave inverted in I and aVL but not in V6

PRECORDIAL LEAD MALPOSITION: abnormal precordial QRS transition

RIGHT HEART OR POSTERIOR LEADS: V3R-V4R or V7-V8-V9

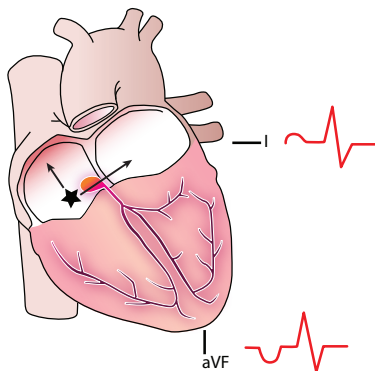
ARTIFACTS: tremor; Parkinson's disease (pseudo-flutter)

SINUS RHYTHM

►► Chapter 6 - Arrhythmias

SINUS RHYTHM (SR): origin of sinoatrial node; HR 60 -100 bpm

- > **Sinus tachycardia:** HR > 100 bpm
- > **Sinus bradycardia:** HR < 60 bpm
- > **Normal atrial activation:** RA to AV node and to LA; P axis 0° to +90° (positive P wave I-II-aVL-aVF); biphasic P wave in V1-V2; duration < 120 ms
- > **Retrograde atrial activation:** retrograde AV conduction or ectopic atrial pacemaker close to AV node; negative P wave in II and aVF



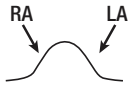
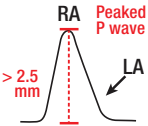
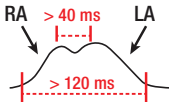
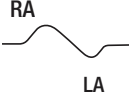
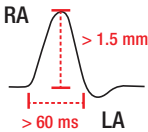
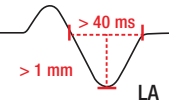
SINUS ARRHYTHMIA: phasic respiratory variation of the duration of the PP interval; variation ≥ 120 ms or $PP_{max} - PP_{min} / PP_{min} > 10\%$

SUPRAVENTRICULAR ARRHYTHMIAS

►► Chapter 6 - Arrhythmias

VENTRICULAR ARRHYTHMIAS

►► Chapter 6 - Arrhythmias

	NORMAL	RA ABNORMALITY	LA ABNORMALITY
II			
V1			
	<ul style="list-style-type: none"> • Axis 60° • Duration < 120 ms 	<ul style="list-style-type: none"> • Axis > 75° 	<ul style="list-style-type: none"> • Axis terminal portion -30° to -90° (negative in III)

INTRA-ATRIAL CONDUCTION BLOCK: Duration of P wave > 120 ms; biphasic P wave in inferior leads; does not satisfy the criteria for RA or LA anomaly

- **Abnormal activation:** RA activation → Bachmann's bundle block → LA activation from coronary sinus (from inferior to superior)

AV CONDUCTION

►► Chapter 6 - Arrhythmias

NORMAL PR INTERVAL: 120-200 ms

LONG PR INTERVAL: PR > 200 ms; 1st degree AV block

SHORT PR INTERVAL: PR < 120 ms in sinus rhythm; rule out accessory pathway

- **Lown-Ganong-Levine syndrome:** atrio-His accessory pathway (James fibers) short-circuiting the AV node; narrow QRS

X:Y AV CONDUCTION: failure of AV node to conduct certain atrial impulses to the ventricle; the refractory period of the AV node is longer when it is stimulated more rapidly (decremental conduction)

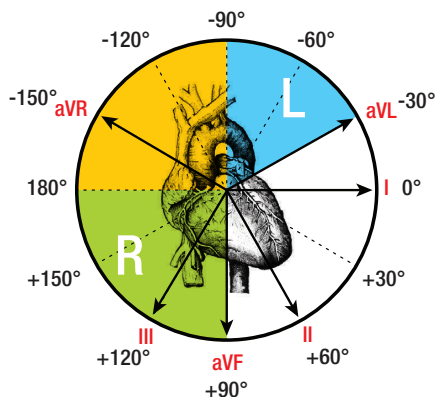
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- **AV block with variable conduction:** 2:1 3:1...; frequent in atrial flutter

AV DISSOCIATION: independent atrial and ventricular rhythms; 3 situations:

- 1) 3rd degree AV block; RR interval > PP interval
- 2) Accelerated junctional rhythm or junctional tachycardia or VT (without retrograde VA conduction); RR < PP; ± fusion or capture beats
- 3) Sinus bradycardia with junctional or ventricular escape (without retrograde VA conduction); RR < PP; ± isorhythmic dissociation

FRONTAL QRS AXIS

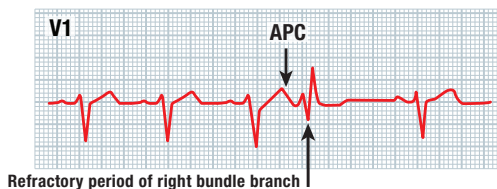


Normal axis	-30° to +90°	I + aVF + (if aVF - → II +)	
Right axis deviation	+90° to +180°	I - aVF +	DDx: RVH; LPHB; dextrocardia; lateral infarction; secundum ASD; vertical heart (COPD); pulmonary embolism
Left axis deviation	-30° to -90°	I + aVF - and II -	DDx: LVH; LAHB; primum ASD; complete AV canal defect; Tricuspid atresia (under-developed RV); pregnancy; ascites; inferior infarction
Extreme "North-West" axis deviation	-90° to 180°	I - aVF -	

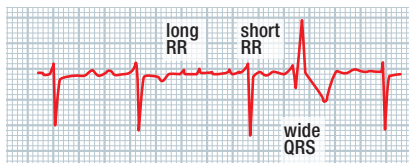
INDETERMINATE AXIS: Equiphasic QRS in all frontal leads (with no dominant QRS); axis perpendicular to the frontal plane

QRS: INTRAVENTRICULAR CONDUCTION

ABERRANT CONDUCTION OF SUPRAVENTRICULAR BEATS: arrival of a supraventricular beat during the relative refractory period of intraventricular conduction tissue; conduction with wide QRS (RBBB > LBBB morphology)



ASHMAN PHENOMENON: Long RR then short RR → wide QRS (frequent RBBB morphology); long RR associated with ↗ refractory period of His-Purkinje tissue



LAHB (LEFT ANTERIOR HEMIBLOCK)

- 1) Left axis deviation -45° to -90°
 - 2) qR in I and aVL
 - 3) rS in III and aVF
 - 4) QRS duration < 120 ms
 - 5) R wave peak time in aVL > 45 ms
 - > Late precordial QRS transition
- > **Rule out differential diagnoses:** LVH; COPD; inferior infarction

LPHB (LEFT POSTERIOR HEMIBLOCK)

- 1) Right axis deviation $+90^\circ$ to $+180^\circ$
 - 2) rS in I and aVL
 - 3) qR in III and aVF
 - 4) QRS duration < 120 ms
- > **Rule out differential diagnoses:** RVH; COPD; lateral infarction; dextrocardia; arm lead reversal

LAHB		LPHB	
I – aVL	III – aVF	I – aVL	III – aVF
<p>aVL: R wave peak time > 45 ms</p>			

LBBB (LEFT BUNDLE BRANCH BLOCK)

- 1) QRS ≥ 120 ms
- 2) Wide monophasic R wave in I-aVL-V5-V6
- 3) Absence of septal q wave in I-V5-V6
- 4) R wave peak time > 60 ms in V5-V6
- 5) ST and T in opposite direction to QRS (appropriate discordance)

Acute myocardial infarction with a LBBB (Sgarbossa criteria)	<ol style="list-style-type: none"> 1) ST elevation ≥ 1 mm in leads with positive QRS (inappropriate concordance) 2) ST depression ≥ 1 mm V1-V2-V3 (inappropriate concordance) 3) ST elevation ≥ 5 mm in leads with negative QRS (extreme discordance)
Old myocardial infarction in LBBB	<ol style="list-style-type: none"> 1) Cabrera's sign: Notch of the upslope of the S wave in V2-V3-V4 2) Chapman's sign: Notch of the upslope of the R wave in V5-V6-I-aVL

INCOMPLETE LEFT BUNDLE BRANCH BLOCK

- 1) QRS 110-119 ms
- 2) LVH pattern
- 3) R wave peak time > 60 ms in V5-V6
- 4) Absence of septal q wave in I-V5-V6

RBBB (RIGHT BUNDLE BRANCH BLOCK)

- 1) QRS ≥ 120 ms
- 3) rsr' , rsR' , or rSR' in V1 or V2 (width of R' or r' > width of r)
- 4) $S > 40$ ms in I and V6 (S larger than R in V6)
 - > In a minority of patients, wide monophasic R wave in V1 and/or V2 (with R wave peak time > 50 ms in V1)
 - > **If axis deviation:** consider bifascicular block (RBBB with LAHB or RBBB with LPHB)
 - > **If bifascicular block with \nearrow PR:** consider lesion of 3 branches with prolonged HV interval

INCOMPLETE RIGHT BUNDLE BRANCH BLOCK

- 1) QRS 110-119 ms
- 2) Other criteria similar to RBBB

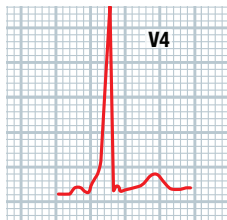
	NORMAL	RBBB	LBBB
V1 V2		 QRS > 120 ms rsr' or rsR' or rSR'	 QRS > 120 ms Deep S wave r wave < 30 ms or absent
V5 V6		 I and V6 : $S \geq 40$ ms	 Prominent wide R wave Absence of septal Q wave R wave peak time > 60 ms

NONSPECIFIC INTRAVENTRICULAR CONDUCTION DISORDER

- 1) QRS > 110 ms
- 2) Absence of criteria of RBBB or LBBB

VENTRICULAR PRE-EXCITATION

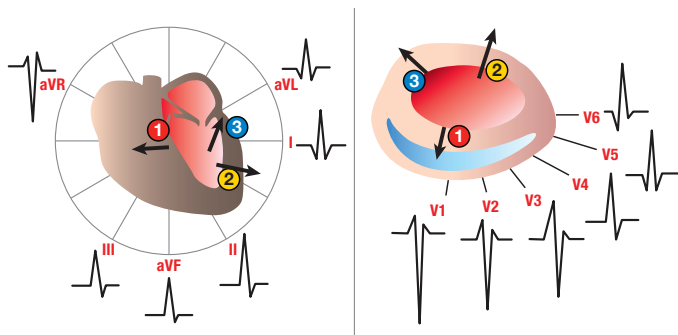
- 1) PR interval < 120 ms (in sinus rhythm)
- 2) **Delta Wave:** slow rise of the initial portion of the QRS
- 3) QRS ≥ 120 ms
- 4) Secondary ST and T anomalies
 - > Possible pseudo-infarction (Q waves)
 - > **Concertina effect:** the degree of pre-excitation can vary according to conduction and the refractory period of the accessory pathway and AV node



SITE OF ACCESSORY PATHWAY	V1	aVF	aVL
Left lateral	+	+	-
Posterior or left septal	+	-	+
Posterior or right septal	-	-	+
Anterior or right lateral	-	+	+

QRS: PRECORDIAL R WAVE TRANSITION

NORMAL VENTRICULAR ACTIVATION: 1) Left-to-right septal activation (septal q wave in I-aVL-V5-V6; septal r wave in aVR and V1); 2) Anterior LV then lateral LV activation; 3) Posterobasal LV activation



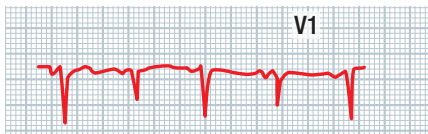
NORMAL PRECORDIAL TRANSITION: rS V1 → qR V6; R = S in V3 or V4

- **DDx of abnormal precordial transition:** lead malposition; dextrocardia; anterior or anteroseptal or posterior myocardial infarction; LVH; RVH; LAHB; LBBB; RBBB; dilated or infiltrative cardiomyopathy; pre-excitation (right or anteroseptal accessory pathway); COPD; pneumothorax; chest wall anomaly...

LOW VOLTAGES: QRS amplitude < 5 mm on frontal leads and < 10 mm on precordial leads

- **DDx:** COPD; obesity; cardiomyopathy; infiltrative disease - amyloidosis - tumor; myocarditis; extensive MI; pericardial effusion; constrictive pericarditis; pleural effusion; myxedema; anasarca; calibration; left pneumothorax

ELECTRICAL ALTERNANS: QRS amplitude varies between beats



- > **DDx:** pericardial effusion; severe cardiomyopathy; severe AR; supraventricular tachycardia
- > **P wave alternans:** pathognomonic of pericardial effusion
- > **T wave alternans:** long QT syndrome

QRS: CHAMBER HYPERTROPHY

LVH		RVH	
V1	V5-V6	V1	V5-V6
↗ S amplitude in V1-V2 ↗ R amplitude in I-aVL-V5-V6 Sokolow & Lyon : $S V1 + R (V5 \text{ or } V6) > 35 \text{ mm}$		Sokolow : $R V1 + S (V5 \text{ or } V6) > 10.5 \text{ mm}$	

LEFT VENTRICULAR HYPERTROPHY (LVH): multiple criteria

- > **Sokolow & Lyon:** $S V1 + R (V5 \text{ or } V6) \geq 35 \text{ mm}$
- > **Cornell voltage:** $S V3 + R aVL \geq 28 \text{ mm}$ (men) and $\geq 20 \text{ mm}$ (women)
- > **R aVL:** $> 11 \text{ mm}$ ($> 18 \text{ mm}$ if left axis deviation)

ROMHILT-ESTES SCORE		
Frontal leads: R or S max $\geq 20 \text{ mm}$ or SV1 or SV2 $\geq 30 \text{ mm}$ or RV5 or RV6 $\geq 30 \text{ mm}$	3 points	≥ 5 points: definite LVH
ST-T abnormality (without Digoxin) ST-T abnormality (with Digoxin)	3 points 1 point	
LA abnormality	3 points	4 points: probable LVH
Left axis deviation (-30° to -90°)	2 points	
QRS duration $\geq 90 \text{ ms}$	1 point	
R wave peak time V5 or V6 $\geq 50 \text{ ms}$	1 point	

- > **Other:** secondary repolarization abnormalities; left axis deviation; LA abnormality; Prolonged R wave peak time in V5-V6

- **LVH associated with LBBB**: consider concomitant LVH if: **A)** LA abnormality; **B)** QRS > 155 ms; **C)** Precordial voltage criteria
- **LVH associated with RBBB**: consider concomitant LVH if: **A)** LA abnormality; **B)** Left axis deviation; **C)** S V1 > 2 mm; **D)** R V5 or V6 > 15 mm; **E)** Left axis deviation and precordial SR max > 29 mm; **F)** R in I > 1 mm

RIGHT VENTRICULAR HYPERTROPHY (RVH): multiple criteria

- **Sokolow**: R V1 + S (V5 or V6) > 10.5 mm
- **R/S V1**: > 1
 - **DDx of prominent R wave in V1-V2**: Lead malposition; Dextrocardia; posterior myocardial infarction; Duchenne muscular dystrophy; RVH (right axis deviation); septal HCM; RBBB; Preexcitation (left posterior or lateral pathway); pediatric ECG
- **R V1**: > 6 mm
- **R wave peak time V1**: > 35 ms
- **R/S V5 or V6**: < 0.75 (V5) or < 0.4 (V6)
- **S V5 or V6**: > 10 mm (V5) or > 3 mm (V6)
- **Other**: Right axis deviation; T wave inversion V1-V2-V3; RA abnormality; S1S2S3; S1Q3
- **RVH associated with RBBB**: consider concomitant RVH if **R in V1 > 15 mm** and right axis deviation

BIVENTRICULAR HYPERTROPHY: look for criteria of both RVH and LVH

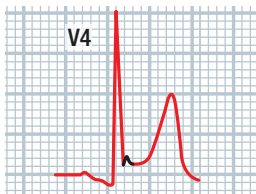
- **LVH**: consider concomitant RVH if → prominent S in V5 or V6; right axis deviation; unusual biphasic R/S complexes on several precordial leads (late precordial transition); RA hypertrophy
- **RVH**: consider concomitant LVH if → combined R/S amplitude in V2 to V4 > 60 mm; LA hypertrophy; prominent R wave in right and left precordial leads

REPOLARIZATION: ST - T - QT - U

ST ELEVATION (AT J POINT IN ≥ 2 CONTIGUOUS LEADS)	
V2 - V3	<ul style="list-style-type: none"> • Men ≥ 40 years: ≥ 2 mm • Men < 40 years: ≥ 2.5 mm • Women: ≥ 1.5 mm
All other leads	≥ 1 mm
V3R - V4R - V7 - V8 - V9	≥ 0.5 mm

DDX OF ST ELEVATION: Myocardial ischemia / STEMI; normal variant (early repolarization); LV aneurysm; pericarditis; myocarditis; cardiomyopathy; Prinzmetal angina / Vasospasm; Takotsubo; LVH; LBBB; pre-excitation; PPM; Brugada syndrome; pulmonary embolism; hyperkalemia; intracranial haemorrhage / SAH; hypothermia (Osborn); post-ECV; lead malposition; hypercalcemia; Rx (class IC AAD)...

- **Early repolarization**: 2-5% of the population; concave ST segment elevation (V2-V3-V4-V5) from J point; notch at J point; prominent T wave



ST DEPRESSION (AT J POINT ON ≥ 2 CONTIGUOUS LEADS) ≥ 0.5 mm (horizontal or descending)

DDX OF ST DEPRESSION: ischemia; LVH; RVH; LBBB; RBBB; pre-excitation; myocarditis; pericarditis; cardiomyopathy; amyloidosis; hypokalemia; Digoxin; pulmonary embolism; intracranial hemorrhage; stroke; acute systemic disease; sepsis; fever; acidosis; anemia; postoperative period after cardiac surgery; hyperventilation...

T WAVE INVERSION (ON ≥ 2 CONTIGUOUS LEADS) ≥ 1 mm; leads with R/S > 1

DDX OF T WAVE INVERSION: persistent juvenile pattern; RBBB; LBBB; pre-excitation; LVH; RVH; apical HCM; ARVD; Brugada; acute CNS lesion; PVC; ventricular pacing ("memory T wave")

> **Persistent juvenile pattern:** T wave inversion in V1-V2-V3 persisting since childhood

GIANT T WAVE INVERSION (>10 MM): Apical HCM; ischemia; Wellens' syndrome; post-STEMI; CNS lesion

> **Wellens' syndrome:** deep T wave inversion in V2-V3-V4 with \nearrow QT interval associated with proximal LAD lesion

SYMMETRICALLY PEAKED T WAVES ≥ 5 mm (frontal leads); ≥ 10 mm (precordial leads)

DDX OF SYMMETRICALLY PEAKED T WAVES: hyperkalemia; acute ischemia (early STEMI); CNS lesion; LVH or LBBB (asymmetrical T waves)

PROLONGED QT INTERVAL $QTc \geq 450$ ms (men) or ≥ 460 ms (women)

DDX OF PROLONGED QT INTERVAL: medication - www.qtdrugs.org (interrupt agent when $QTc > 500$ ms or increases by > 60 ms); long QT syndrome; hypocalcemia; hypokalemia; hypomagnesemia; hypothermia; CNS lesion; ischemia; severe bradycardia... **+**

> **Normal QT:** $< 1/2$ RR interval

• **Bazett's equation:** $QTc = QT \text{ (msec)} / \sqrt{R-R \text{ (s)}}$ (HR < 100 bpm) **+**

• **Linear model:** $QTc = QT + 1.75 \times (HR - 60)$

• **Significant change on medication:** > 60 ms

> **Measurement of QT:** longest interval (often V2-V3); draw a tangent from the most pronounced descent of the T wave to intersect the TP segment

> **QT associated with prolonged QRS:** JTC interval (QT duration - QRS duration) (normal < 370 ms)

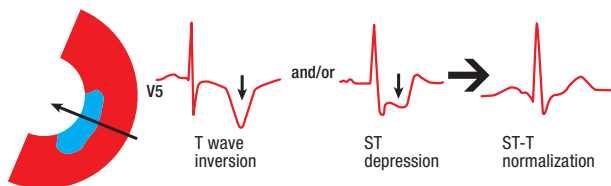
SHORT QT INTERVAL: $QTc \leq 390$ msec (HR < 100 bpm) **+**

> **Etiologies:** hypercalcemia; hyperkalemia; Digoxin; congenital short QT syndrome

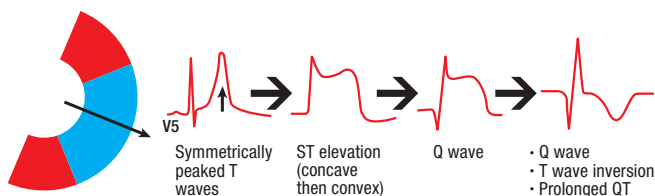
PROMINENT U WAVE (> 2 MM): hypokalemia; hypercalcemia; Digoxin; class IA and IC AAD; thyrotoxicosis; intracranial hemorrhage; congenital long QT syndrome

> **U wave inversion:** leads on which the T wave is positive; sign of ischemia

SUBENDOCARDIAL ISCHEMIA



TRANSMURAL ISCHEMIA



ST ELEVATION OR SYMMETRICALLY PEAKED T WAVES

V1-V2	Anteroseptal infarction
V3-V4	Anteroapical infarction
V5-V6 (\pm aVL - I)	Anterolateral infarction
V1-V2-V3-V4-V5-V6	Extensive anterior infarction
aVL-I	Lateral infarction
II-III-aVF	Inferior infarction
V3R-V4R (\pm V1) (+ II-III-aVF)	RV infarction
V7-V8-V9 (mirror changes in V1-V2)	Posterior infarction

ABNORMAL Q WAVE (IN ≥ 2 CONTIGUOUS LEADS)

V2-V3	QS or Q duration ≥ 20 ms
I-II-aVL-aVF V4-V5-V6 V7-V8-V9	QS or Q ≥ 30 ms and > 1 mm
V1-V2	Consider old posterior infarction if R > 40 ms with R/S ≥ 1 in absence of conduction disorder

DDX OF Q WAVES (PSEUDO-INFARCTION): septal Q waves (V4-V5-V6; I; aVL; aVF); normal variant in V1 or III; LVH; RVH; LBBB; LAHB; pre-excitation; myocarditis; RCM - Infiltration (amyloidosis; sarcoidosis; tumor); HCM; DCM; dextrocardia; hyperkalemia; chest deformity; pneumothorax; COPD; pulmonary embolism...

CLINICAL ENTITIES

ACUTE PERICARDITIS: 4 phases

- 1) Diffuse ST elevation (concave); PR segment depression; mirror image in aVR
- 2) Normalisation of ST segment with depression of J point
- 3) T wave inversion
- 4) Normalisation of T waves

PERICARDIAL EFFUSION: low voltage; electrical alternans

PULMONARY EMBOLISM: sinus tachycardia; QR or qR in III-aVF / V1-V2-V3 (pseudo-infarction); S1Q3T3 (12% of patients); ST depression (sometimes elevation) and T wave inversion in V1-V2-V3; complete or incomplete RBBB; delayed precordial QRS transition; right axis deviation

HYPERTROPHIC CARDIOMYOPATHY (HCM): LVH; LAH; left axis deviation; pseudo-infarction (Q waves - inferior - lateral - precordial leads); giant T wave inversion in precordial leads (apical HCM)

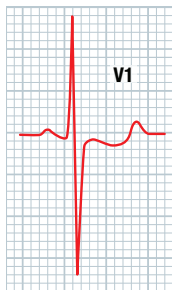
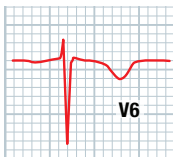
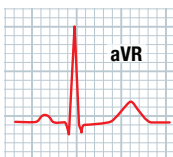
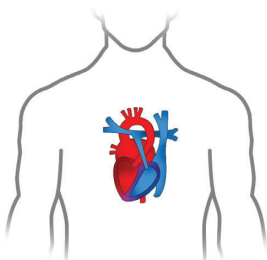
PRIMUM ASD: RBBB; left axis deviation; RAH

SECUNDUM ASD: Incomplete RBBB; right axis deviation; RAH; notch in the upslope of the R wave in inferior leads

MITRAL STENOSIS: RVH; right axis deviation; LAH \pm RAH

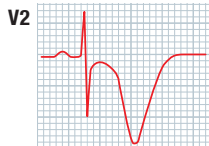
LEFT VENTRICULAR ANEURYSM: persistent convex ST elevation (3 weeks post-MI) in the presence of a Q wave

DEXTROCARDIA: inverted P and QRS and T waves in I and aVL; positive QRS in aVR; inverted precordial QRS transition



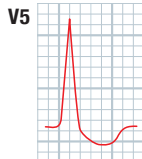
COPD: RVH; RAH; right axis deviation; \searrow QRS amplitude on frontal leads (electrical isolation due to hyperinflation); delayed precordial transition (cardiac position modified by hyperinflation and lowering of the diaphragm); persistent S wave in all precordial leads; low amplitude R wave in V6; pseudoinfarction (Q waves); MAT - APCs - AF - Flutter

ACUTE CNS LESION: giant T wave inversions on precordial leads (sometimes positive and prominent);
 ↗ QT interval; U waves; transient ST elevation; ± Torsade de pointes



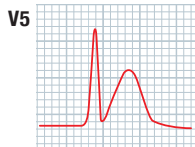
DIGOXIN IMPREGNATION:

scooped ST;
 flattened T wave; ↘ QT interval;
 ↗ PR interval; U wave

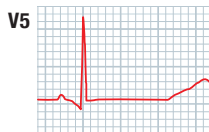


DIGOXIN TOXICITY: sinus bradycardia; sinus arrest; ectopic atrial tachycardia; "regularized" AF (junctional escape rhythm); junctional tachycardia; AV block; PVCs; VT; bidirectional VT; VF

HYPERCALCEMIA: ↘ QT interval; sharp T wave upstroke; ↗ PR interval

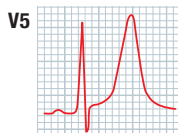


HYPOCALCEMIA: ↗ QT interval (due to ↗ ST interval; T wave unchanged)

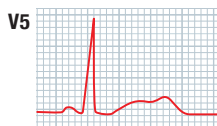


HYPERKALEMIA: symmetrically peaked

T waves; ↘ QT interval →
 ↗ QRS duration and ↗ PR interval;
 conduction disorders (RBBB; LBBB;
 bifascicular block; AV block) → **flattened P wave** (or even loss of P wave with sinoventricular rhythm; unexcitable atrial muscle); ST elevation → ventricular flutter / sinusoidal rhythm → asystole



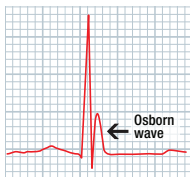
HYPOKALEMIA: prominent U wave;
 ST depression; flat T wave; ↗ QT interval;
 blocks; atrial - ventricular - junctional tachyarrhythmias / Torsade de pointes



HYPOTHERMIA (< 34°C): Osborn wave; bradycardia; ↗ QT interval; ↗ QRS duration; ↗ PR interval; artefacts secondary to rigors; junctional bradycardia; ventricular arrhythmia; asystole

➤ **Osborn wave:** notch and elevation of J point (maximal in V5-V6)

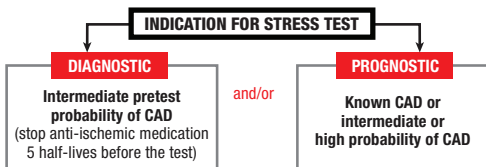
V5



HYPOTHYROIDISM: low voltage; sinus bradycardia; flat T wave; ↗ PR interval; conduction disorders; ↗ QT interval

1.3/ STRESS TEST

INDICATION



	SENSITIVITY	SPECIFICITY
General population	68 %	77 %
LMCA or 3-vessel disease	86 %	53 %

CONTRAINDICATIONS

ABSOLUTE	RELATIVE
<ul style="list-style-type: none"> Acute infarction ≤ 48 h High-risk unstable angina Decompensated heart failure Uncontrolled arrhythmia with symptoms or hemodynamic instability Myocarditis or acute pericarditis Severe symptomatic aortic stenosis Acute pulmonary embolism Acute aortic dissection 	<ul style="list-style-type: none"> Left main coronary artery stenosis Moderate stenotic valvular heart disease Electrolyte disorders Severe HTN: > 200/110 mmHg Tachyarrhythmia or bradyarrhythmia HCM Advanced AV block Mentally unable to perform the exercise <p>ANOMALIES ON BASELINE ECG</p> <ul style="list-style-type: none"> Pre-excitation LBBB Ventricular pacing ST depression > 1 mm Digoxin and LVH with repolarization abnormalities (false-positive)

COMPLICATIONS: 3.5 infarctions - 4.8 arrhythmias - 0.5 deaths per 10,000 examinations performed

PROTOCOLS

STAGE	% SLOPE	SPEED (mph)	TIME (min)	VO ₂ (mL/kg/min)	METs
BRUCE PROTOCOL					
0	0	1.7	-6 to -3		
0.5	5	1.7	-3 to 0	11	3
1	10	1.7	3	17	4.5
2	12	2.5	6	25	7
3	14	3.4	9	35	10
4	16	4.2	12	47	13
CORNELL PROTOCOL					
1	0	1.7	2	7	2
2	5	1.7	4	11	3
3	10	1.7	6	17	4.5
4	11	2.1	8	19	5.5
5	12	2.5	10	25	7
6	13	3	12	30	8.5
7	14	3.4	14	35	10
8	15	3.8	16	40	11.5
9	16	4.2	18	47	13
NAUGHTON PROTOCOL					
1	0	2	2	7	2
2	3.5	2	4	10.5	3
3	7	2	6	14	4
4	10.5	2	8	17.5	5
5	14	2	10	21	6
6	17.5	2	12	24.5	7
7	12.5	3	14	28	8

1 MET: = 3.5 mL O₂/kg/min (O₂ consumption in a resting subject)



ESTIMATED VO₂: = [(2.68 x mph) x (0.1 + (% slope x 1.8))] + 3.5

MONITORING: ECG - HR - BP - Rating of perceived exertion (Borg scale) at the end of each stage; at the end of exercise; every 2-3 min during recovery (for 6-10 min or normalization of ECG)

BRUCE PROTOCOL: change of speed and slope at each 3-min stage; modified Bruce with the addition of 2 initial stages if necessary

CORNELL PROTOCOL: more gradual increase of exertion (each Bruce stage is subdivided into 2 substages)

NAUGHTON PROTOCOL: 2-min stages; increase of 1 MET per stage; used during evaluation of VO₂ max

RAMP PROTOCOL: the slope and speed increase progressively according to the patient's previously estimated functional class (according to an activity scale expressed in METs) to achieve exercise lasting about 8 to 12 minutes

POST-INFARCTION: **A)** Prescription of physical activity; **B)** Effects of treatment; **C)** Prognostic value (unknown coronary anatomy)

> **Submaximal stress test (3-4 days):** Modified Bruce or Naughton; stop if HR ≥ 120 bpm or $\geq 70\%$ of predicted HRmax or 5 METs or Angina or Dyspnea or \searrow ST 2 mm or \searrow BP or ≥ 3 consecutive PVCs

> **Stress test limited by symptoms (3 weeks):** standard test

ELECTROCARDIOGRAPHIC EVALUATION

ST SEGMENT: depression compared to PQ segment, **80 ms from point J (ST80)** or 60 ms from point J if HR > 130 bpm (ST60)



Normal response: ascending ST depression	<ul style="list-style-type: none"> ST80 depression < 1.0 mm Ascending slope ≥ 1 mV/s (1 mV = 10 mm) 	<p>ST80</p>
Abnormal response: horizontal ST depression	<ul style="list-style-type: none"> J and ST80* depression ≥ 1 mm Horizontal slope (< 0.7 to 1 mV/s) 	<p>3 BEATS</p>
Abnormal response: descending ST depression	<ul style="list-style-type: none"> J and ST80* depression ≥ 1 mm Descending slope (< -1 mV/s) 	<p>3 BEATS</p>
Gray zone: ST depression with slow rise	<ul style="list-style-type: none"> ST80 depression ≥ 1.0 mm Ascending slope ≥ 1 mV/s Evaluate according to the patient's pretest probability of CAD 	<p>ST80</p> <p>Slope = 3 mV/s</p>
Transmural ischemia: ST elevation	<ul style="list-style-type: none"> J and ST60 elevation ≥ 1 mm Absence of Q wave Localize ischemia 	<p>3 BEATS</p>

* ST60 if HR > 130 bpm

MORE SPECIFIC LEADS: **V4-V5-V6;** isolated ST abnormalities in II and aVF often associated with false-positive results

ST DEPRESSION: does not localize the ischemia

ST ELEVATION IN AVR: associated with left main coronary / ostial LAD stenosis

U WAVE INVERSION: associated with significant CAD

BASELINE RBBB: ignore leads V1-V2-V3-V4 during the stress test

FALSE-POSITIVE: baseline ST abnormality; anemia; cardiomyopathy; Digoxin; hyperventilation; hypokalemia; intraventricular conduction disorders; LVH; pre-excitation; severe AS; severe HTN; severe hypoxia; severe volume overload; supraventricular tachycardia; MVP

INDICATIONS TO TERMINATE THE TEST

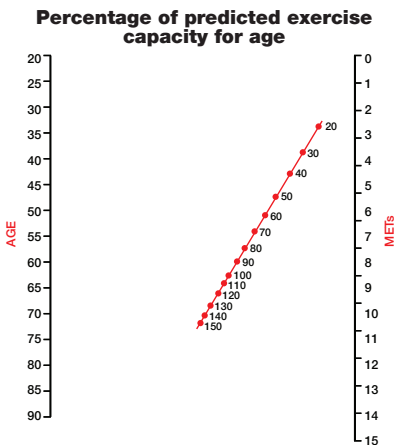
ABSOLUTE	RELATIVE
<ul style="list-style-type: none"> • \searrow BP \geq 10 mmHg with ischemia • Severe and intolerable angina (CCS 3 to 4/4 on tolerance scale) • Ataxia; Faintness • Hypoperfusion (cyanosis; pallor) • Technical difficulty • Patient wants to stop • Sustained VT • ST elevation: \geq 1 mm (in absence of Q wave and elsewhere than in aVR or V1) 	<ul style="list-style-type: none"> • \searrow BP \geq 10 mmHg • ST depression: $>$ 2 mm • Marked change of QRS axis • Arrhythmia: polymorphic PVCs; triplet PVCs; supraventricular tachycardia; block; bradyarrhythmia • Fatigue - Dyspnea - Wheezing - Leg cramps - Claudication • Intraventricular conduction disorder unable to be distinguished from VT • Worsening retrosternal chest pain • Exaggerated hypertensive response: BP $>$ 250/115

OTHER ELEMENTS TO BE EVALUATED

NON-DIAGNOSTIC TEST: insufficient exercise ($<$ 85% of predicted HRmax for age) +

> Predicted HRmax for age: $= 220 - \text{age}$

MAXIMUM FUNCTIONAL CAPACITY: # METs; powerful prognostic marker



Source: Morris CK, Myers J, Froelicher VF, et al. JACC 1993; 22; 175-182.

DOUBLE PRODUCT: $HR \times SBP / 1000$ (normal: 20-35 mmHg x bpm x 10^{-3})

ANGINA: generally occurs after ST abnormalities

SYSTOLIC BLOOD PRESSURE: peak generally observed between 160 and 200 mmHg

- > **Abnormal response:** failure to reach 120 mmHg or $\searrow > 10$ mmHg or \searrow below baseline SBP; associated with significant ischemia or cardiomyopathy or LVOT obstruction or antihypertensive medication or significant dehydration
- > **Exaggerated hypertensive response:** SBP > 210 mmHg in men or > 190 mmHg in women; risk of developing HTN in the future in a currently normotensive patient; indicates an insufficient reduction of systemic vascular resistance by arteries and arterioles during exercise; ABPM may be indicated

CHRONOTROPIC INCOMPETENCE: failure to achieve > 80 -85% of predicted HRmax for age (with significant exercise); associated with poor prognosis

- > **Chronotropic index:** observed HR reserve (maximum HR on stress test - HR at rest) / (predicted HRmax for age - HR at rest); chronotropic incompetence if < 80 %

DE NOVO LBBB ON EXERTION: associated with \nearrow risk of mortality and significant CAD

RECOVERY OF HR AT 1 MIN: = peak HR - HR after 1 minute of rest

- > **Abnormal HR recovery:** < 12 bpm (standing) or 18 bpm (supine); associated with poor prognosis

PVCS DURING RECOVERY: associated with \nearrow risk of mortality (compared to patients with PVCs on exertion only)

DUKE TREADMILL SCORE (DTS)

DTS = EXERCISE TIME (MIN) - (5 X MAXIMUM ST DEPRESSION IN MM) - 4 X (ANGINA SCORE)	
ANGINA SCORE <ul style="list-style-type: none"> • Angina requiring termination = 2 • Angina not requiring termination = 1 • No angina = 0 	ONE-YEAR MORTALITY <ul style="list-style-type: none"> • DTS ≤ -11 and less: 5.0% • DTS between +4 and -10: 1.25% • DTS $\geq +5$: 0.25 %

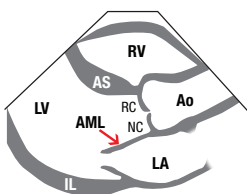
Mark DB, Hlatky MA, Harrell FE Jr et al. Ann Intern Med. 1987; 106:793.

FACTORS OF POOR PROGNOSIS

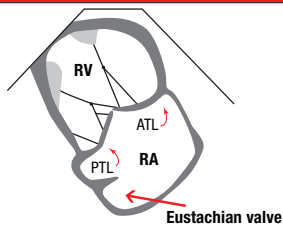
DUKE TREADMILL SCORE: ≤ -11 and less	+
LOW FUNCTIONAL CAPACITY: < 5 METs	+
LOW THRESHOLD ANGINA OR ISCHEMIA: $< 70\%$ predicted HRmax or HR < 120 bpm or ≤ 4 METs	+
SEVERE ST DEPRESSION: ≥ 2 mm	+
MULTIPLE LEADS: ischemia on ≥ 5 leads	+
PERSISTENCE: ischemia ≥ 3 min during recovery	+
ST ELEVATION: ≥ 1 mm (except for aVR)	+
ABNORMAL BP RESPONSE: failure to achieve 120 mmHg or $\searrow > 10$ mmHg or \searrow below baseline SBP	
SUSTAINED OR SYMPTOMATIC VT	

1.4/ TRANSTHORACIC ECHOCARDIOGRAPHY (TTE)

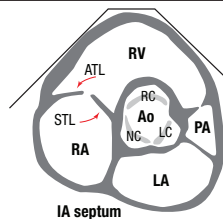
PARASTERNAL - LONG AXIS (PLAX)



PARASTERNAL - RV INFLOW TRACT

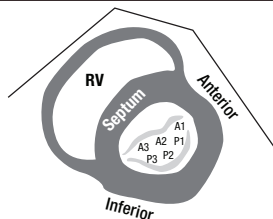


SHORT AXIS - AORTIC VALVE LEVEL

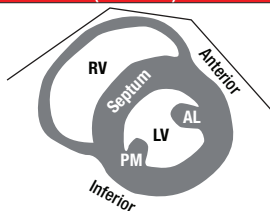


IA septum

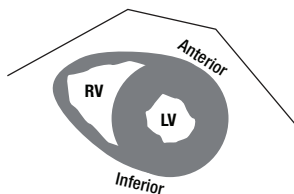
SHORT AXIS - MITRAL VALVE LEVEL



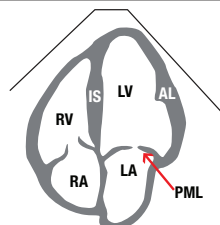
**SHORT AXIS - MITRAL PAPILLARY MUSCLES
(MID 1/3 LV)**



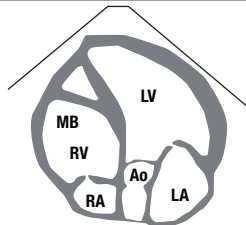
SHORT AXIS - APICAL

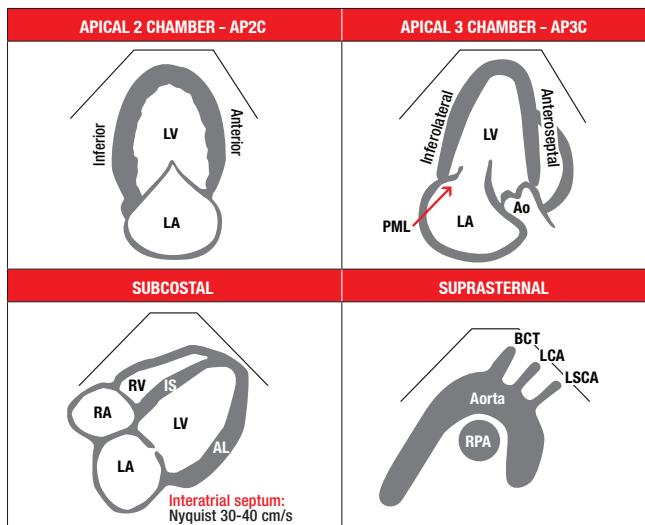


APICAL 4 CHAMBER - AP4C



APICAL 5 CHAMBER - AP5C





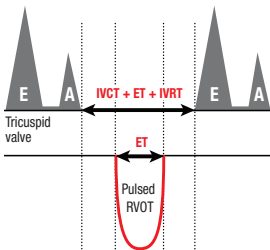


LV - RV - LA - RA - PA EVALUATION

	LEFT VENTRICLE			
	NORMAL	SLIGHTLY ABNORMAL	MODERATELY ABNORMAL	SEVERELY ABNORMAL
LVDD: Diastolic diameter (mm)	F: 38-52 M: 42-58	F: 53-56 M: 59-63	F: 57-61 M: 64-68	F: ≥ 62 M: ≥ 69
LVSD: Systolic diameter (mm)	F: 22-35 M: 25-24	F: 36-38 M: 41-43	F: 39-41 M: 44-45	F: ≥ 42 M: ≥ 46
Indexed diastolic volume (mL/m²)	F: 29-61 M: 34-74	F: 62-70 M: 75-89	F: 71-80 M: 90-100	F: ≥ 81 M: ≥ 101
Index systolic volume (mL/m²)	F: 8-24 M: 6-10	F: 25-32 M: 32-38	F: 33-40 M: 39-45	F: ≥ 41 M: ≥ 46
Interventricular septum (mm)	F: 6-9 M: 6-10	F: 10-12 M: 11-13	F: 13-15 M: 14-16	F: ≥ 16 M: ≥ 17
Posterior wall (mm)	F: 6-9 M: 6-10	F: 10-12 M: 11-13	F: 13-15 M: 14-16	F: ≥ 16 M: ≥ 17
Indexed LV mass (g/m²) by linear method	LV mass = 0.6 g + 0.8 x (1.04 x [(LVDD + PW + Septum)³ - LVDD³])			
	F: 43-95 M: 49-115	F: 96-108 M: 116-131	F: 109-121 M: 132-148	F: ≥ 122 M: ≥ 149

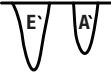

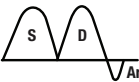

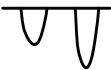



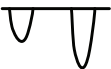



Relative wall thickness (RWT)	RWT = 2 x PW / LVDD			
	F: 0.22-0.42 M: 0.24-0.42	F: 0.43-0.47 M: 0.43-0.46	F: 0.48-0.52 M: 0.47-0.51	F: ≥ 0.53 M: ≥ 0.52
	CONCENTRIC REMODELING Indexed mass: ≤ 95 g/m ² (F) and ≤ 115 g/m ² (M) RWT > 0.42		CONCENTRIC LVH Indexed mass: > 95 g/m ² (F) and > 115 g/m ² (M) RWT > 0.42	
	NORMAL GEOMETRY Indexed mass: ≤ 95 g/m ² (F) and ≤ 115 g/m ² (M) RWT ≤ 0.42		ECCENTRIC LVH Indexed mass: > 95 g/m ² (F) and > 115 g/m ² (M) RWT ≤ 0.42	
LVEF (%) (Simpson biplane)	LVEF = ED volume - ES volume / ED volume			
	F: 54-74 M: 52-72	F: 41-53 M: 41-51	30-40	< 30
LVEF (%) (Dumesnil)	LVEF = stroke volume / ED volume • Stroke volume = 0.785 x LVOT diameter ² x LVOT VTI • ED volume = 7 x LVDD ³ / (2.4 + LVDD)			
Endocardial shortening fraction (%)	% shortening = LVDD - LVSD / LVDD			
	F: 27-45 M: 25-43	F: 22-26 M: 20-24	F: 17-21 M: 15-19	F: ≤ 16 M: ≤ 14
Cardiac output (L/min)	• CO = HR x (0.785 x LVOT diameter² x LVOT VTI) • CO = HR x (ED volume - ES volume)			
	Normal cardiac output : 4 - 6 L/min			
dP/dt (isovolumic contraction)	dP/dt = 32 / time for velocity of MR jet to increase from 1 m/s to 3 m/s			
	Normal dP/dt: > 1200 mmHg/sec			
LIMP (Left MPI)	LIMP = IVCT + IVRT / ET ejection time			
	• Global myocardial performance index • ▶▶ RV MPI (right ventricle) • Normal LV MPI : < 0.39 ± 0.05			
RIGHT VENTRICLE				
RV dilatation (qualitative; AP4C)	Size of RV < size of LV; apex belongs to LV	Size of RV similar to size of LV; apex belongs to LV	Size of RV similar to size of LV; apex shared between the two	RV > LV; apex belongs to RV

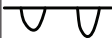

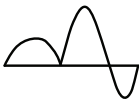
Basal RV diameter AP4C (mm)	Dilatation: > 41 mm	RV-focused apical 4-chamber view; LV apex centered and not truncated, while displaying the largest basal RV diameter
Mid-cavity RV diameter AP4C (mm)	Dilatation: > 35 mm	
Longitudinal RV diameter AP4C (mm)	Dilatation: > 83 mm	
RVOT diameter (mm)	<ul style="list-style-type: none">• Proximal: PLAX (dilatation if > 30 mm) or PSAX above the Ao valve (dilatation if > 35 mm)• Distal: PSAX above the P valve (dilatation if > 27 mm)	
RV wall thickness (mm)	RVH: > 5 mm Subcostal; end-diastole; at the extremity of T valve leaflets	
Septal curvature	Pressure overload D-shaped septum in systole and diastole 	Volume overload D-shaped septum in diastole 
FAC: RV fractional area change (%)	RV systolic dysfunction: < 35%	FAC = (end-diastolic area - endsystolic area) / end-diastolic area x 100% AP4C; include the trabeculae in the cavity
RV S' (Tissue Doppler)	RV systolic dysfunction: < 9.5 cm/s	AP4C; Velocity of longitudinal systolic excursion of basal segment of the free wall of the RV; angle dependant
TAPSE (tricuspid annular plane systolic excursion)	RV systolic dysfunction: < 17 mm	AP4C; RV longitudinal function; Tricuspid lateral annular longitudinal excursion by M-mode (mm)

RIMP (Right MPI): Global myocardial performance index	Tissue Doppler: RV dysfunction if > 0.54 Pulsed Doppler: RV dysfunction if > 0.43	RIMP = IVCT + IVRT / ET ejection time • Tissue Doppler: tricuspid annulus: ET = duration S'; IVCT + IVRT + ET = interval between the end of A' and the start of E' • Pulsed Doppler: 		
LEFT AND RIGHT ATRIA				
LA diameter PLAX (mm)	F: 27-38 M: 30-40	F: 39-42 M: 41-46	F: 43-46 M: 47-52	F: ≥ 47 M: ≥ 52
Indexed LA volume (mL/m²)	LA volume = (0.85 x A1 x A2) / L Area and long axis on biplane views (AP4C and AP2C)			
	16-34	35-41	42-48	≥ 48
Indexed RA volume (mL/m²)	RA volume = RA area² / L (AP4C, single-plane) Normal: F: 21 ± 6 M: 25 ± 7			
Indexed RA length AP4C (cm/m²)	Long axis (parallel to the interatrial septum) Normal: F: 2.5 ± 0.3 M: 2.4 ± 0.3			
Indexed RA diameter AP4C (cm/m²)	Short axis (lateral wall of RA to interatrial septum) Normal: 1.9 ± 0.3			
RA pressure (CVP) estimated by subcostal view of inferior vena cava (mmHg)	<ul style="list-style-type: none">• IVC ≤ 21 mm and collapse > 50%: RA pressure = 3 mmHg (0-5 mmHg)• IVC > 21 mm and collapse < 50%: RA pressure = 15 mmHg (10-20 mmHg)• Intermediate: RA pressure = 8 mmHg (5-10 mmHg)• Ventilated patient: IVC ≤ 12 mm associated with RA pressure < 10 mmHg			
PULMONARY ARTERY				
Systolic PAP (mmHg)	sPAP = 4 x TR pressure gradient² + RA pressure In the absence of RVOT obstruction			
	< 35	35 - 50	50 - 80	> 80
Diastolic PAP (mmHg)	dPAP = 4 x PR end-diastolic velocity² + RA pressure			

Mean PAP (mmHg)	<ul style="list-style-type: none"> • $mPAP = 1/3 sPAP + 2/3 dPAP$ • $mPAP = 4 \times \text{early diastolic PR velocity}^2 + \text{RA pressure}$ • Mahan: $mPAP = 79 - (0.45 \times \text{PA acceleration time})$ <ul style="list-style-type: none"> > If PA acceleration time < 120 ms: $mPAP = 90 - (0.62 \times \text{PA acceleration time})$ > PA acceleration time: start of QRS to peak pulmonary flow velocity; pulsed Doppler 			
Pulmonary artery diameter (mm)	15-21	22-25	26-29	≥ 30

DIASTOLIC FUNCTION

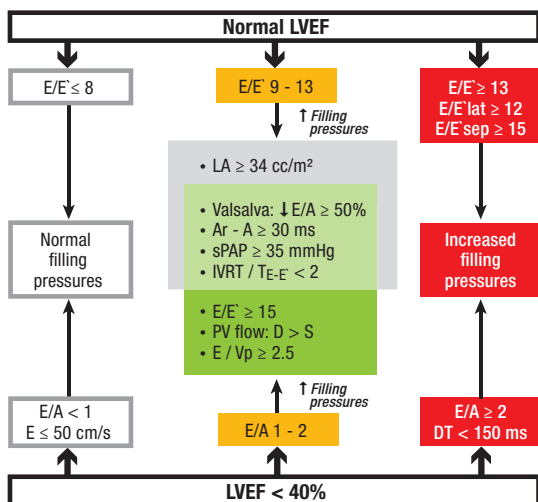
DIASTOLIC FUNCTION - GRADING					
	E' (cm/s) E/E'	LA (mL/m ²)	E/A DT (ms) IVRT (ms)	PV FLOW AR - A (ms)	VALSALVA
NORMAL PATTERN	E'sep ≥ 8 E'lat ≥ 10 E/E' ≤ 8 	< 34	E/A 0.8 - 1.5 DT 160-200 	PV S > D Ar - A < 0 	Reduction of E/A ratio < 0.5 
GRADE I: ABNORMAL RELAXATION PATTERN	E'sep < 8 E'lat < 10 E/E' ≤ 8 	≥ 34	E/A < 0.8 DT > 200 IVRT ≥ 100 	PV S > D Ar - A < 0 	Reduction of E/A ratio < 0.5 
Normal filling pressures (generally)					
> 60 years: E/A < 1 and DT > 200 ms in the absence of LVH or heart disease → normal for age					
GRADE II: PSEUDO-NORMAL PATTERN	E'sep < 8 E'lat < 10 E/E' 9-12 	≥ 34	E/A 0.8 - 1.5 DT 160-200 	VP D > S Ar - A ≥ 30 	Reduction of E/A ratio ≥ 0.5 
↗ Filling pressures					

GRADE III: RESTRICTIVE PATTERN	$E_{sep} < 8$ $E'_{lat} < 10$ $E/E' > 13$ $E/E_{sep} \geq 15$ $E/E'_{lat} > 12$	≥ 34	$E/A \geq 2$ $DT < 160$ $IVRT \leq 60$	$PV D > S$ $Ar - A \geq 30$	Variable
					
					
					
↗ ↗ ↗ Filling pressures DDx: Severe decompensated heart failure; advanced RCM; severe CAD; severe acute AR; Constrictive pericarditis					
IIla: filling pattern improves in response to treatment IIlb: absence of improvement of the filling pattern in response to treatment					

IVRT: Continuous Doppler LVOT; interval between end of Ao ejection and start of mitral filling (E wave)

FUSION OF E AND A: E wave > 20 cm/s at the beginning of the A wave

FILLING PRESSURES



- > **Increased filling pressures:** Wedge pressure > 12 mmHg or LVEDP > 16 mmHg
- > **TE-E'** = (interval between QRS and onset of E) - (interval between QRS and onset of E')
- > **Vp:** velocity of propagation of diastolic flow on color M-mode
- > **AF:** ↗ filling pressures if **IVRT ≤ 65 ms or DT of pulmonary vein diastolic flow ≤ 220 ms or septal E/E' ≥ 11**



LEFT VENTRICLE: divided into 16 segments (+ apical cap)

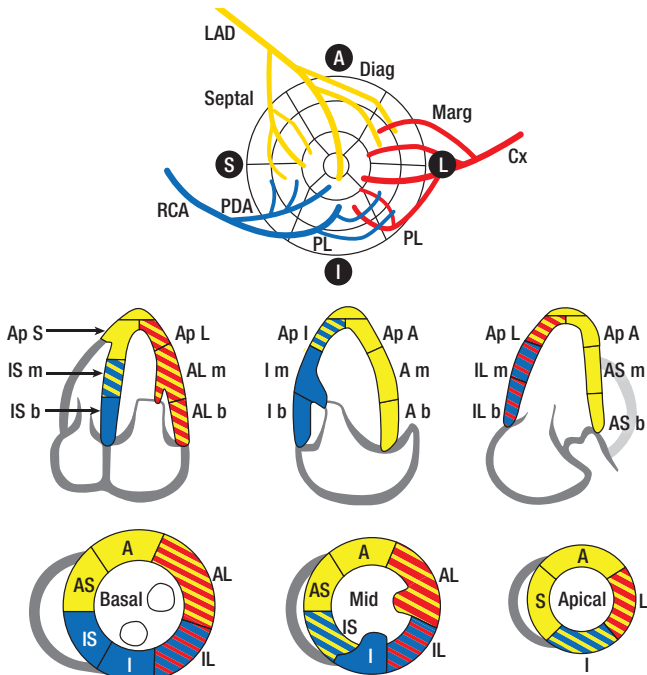
- > **Interventricular septum:** between the attachments of the RV to the LV

LEFT VENTRICULAR CHAMBER: 3 levels → **A)** Base - **B)** Mid 1/3 (papillary muscles) - **C)** Apex

SEGMENTAL WALL MOTION: evaluate endocardial excursion and segmental thickening +

- 1 - NORMAL (or hyperdynamic)	- 2 - HYPOKINESIA	- 3 - AKINESIA	- 4 - DYSKINESIA	- 5 - ANEURYSM
Thickening > 40% in systole	Thickening 10-40%	Thickening < 10% (negligible)	Paradoxical systolic movement	Diastolic deformity

WMSI = Sum of each segment / Number of segments evaluated
 Normal = 1; WMSI > 1.7 associated with perfusion defect > 20% (MIBI)



VALVULAR HEART DISEASE

AORTIC STENOSIS		SEVERE
Maximum jet velocity	Look for parallel alignment between continuous Doppler and the jet	> 4 m/s
Mean gradient	Mean of instantaneous mean gradients during ejection	> 40 mmHg
Valve area by continuity equation	Aortic valve area = $0.785 \times \text{LVOT diameter}^2 \times \text{LVOT VTI} / \text{Aortic valve VTI}$	< 1 cm ²
	<ul style="list-style-type: none"> • LVOT VTI and LVOT diameter obtained at the same distance from the valve • Proximal velocity (LVOT) > 1.5 m/s: use peak velocity and maximum gradient to grade severity • Maximum gradient = 4 (maximum v² – proximal v²) 	
LVOT VTI / Ao valve VTI ratio	Independent of measurement of LVOT	< 0.25
Velocity > 4 m/s and Area > 1 cm²: high output; significant AR; tall patient Velocity < 4 m/s and Area < 1 cm²: low output; small patient; significant MR		

MITRAL STENOSIS		SEVERE
Mean gradient	Mean of instantaneous mean gradients during filling	> 10 mmHg
Valve area by planimetry	<ul style="list-style-type: none"> • Method of choice in rheumatic MS • At the extremity of the leaflets (PSAX) 	< 1 cm ²
Valve area by pressure half-time	Mitral valve area = 220 / PHT	< 1 cm ²
	<ul style="list-style-type: none"> • Use the slope of the E wave at mid-diastole • Method of choice in rheumatic MS • Caveats: immediately after balloon valvuloplasty; severe AR (short PHT); abnormal LV relaxation (long PHT); ⚡ LVEDP (short PHT); prosthetic valve (do not calculate prosthetic area but report PHT) 	
Valve area by continuity equation	Mitral valve area = $0.785 \times \text{LVOT diameter}^2 \times \text{LVOT VTI} / \text{mitral valve VTI}$	< 1 cm ²
Valve area by PISA	Mitral valve area = $[6.28 \times \text{PISA radius} \times \text{Aliasing velocity} / \text{Peak MS velocity}] \times \alpha/180^\circ$	< 1 cm ²

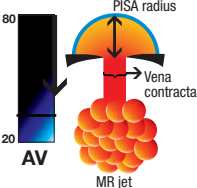
INDICATE HR AT THE TIME OF MEASUREMENTS; EVALUATE PAP

BVR SCORE – BALLOON VALVULOPLASTY REGISTRY (WILKINS SCORE)				
	– 1 – Mobility of leaflets	– 2 – Thickening of leaflets	– 3 – Calcification of leaflets	– 4 – Thickening of subvalvular apparatus
1 point	Very mobile valve; restriction of the extremity of the leaflets	Leaflets measure 4-5 mm	A single hyperechodense zone	Minimal thickening under the leaflets

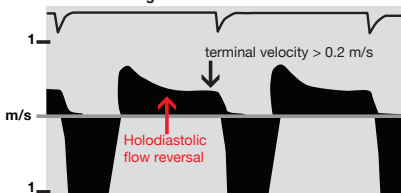
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Cardiac diagnostic assessment

2 points	Normal mobility of the base and middle parts of the leaflets	Localized thickening (5-8 mm)	Several localized hyperechodense zones on the leaflets	Thickening of the chordae (1/3 of their length)
3 points	Mobility of the base of the valve	Thickening of all of the leaflet (5-8 mm)	Hyperechodensities as far as the middle portion of the leaflets	Thickening of the chordae as far as their distal third
4 points	Minimal or absent movement of the leaflets	Considerable thickening of the entire leaflet (8-10 mm)	Extensive hyperechodensities on the majority of the leaflets	Severe thickening as far as the papillary muscles
Score ≤ 8 associated with a favorable result of balloon valvuloplasty				

MITRAL REGURGITATION		SEVERE
Vena contracta	Narrowest portion of the jet distal to the regurgitating orifice; avoid AP2C; Nyquist 50-60 cm/s	$\geq 7 \text{ mm}$
Regurgitant volume	<p>VOLUMETRIC METHOD</p> <p>Regurgitant volume = $(0.785 \times \text{Mitral annulus diameter}^2 \times \text{antegrade mitral VTI}) - (0.785 \times \text{LVOT diameter}^2 \times \text{LVOT VTI})$</p> <ul style="list-style-type: none"> Mitral annulus diameter: mean of PLAX and AP4C Significant AR: use pulmonic valve flow <p>PISA: Regurgitant volume = EROA x MR VTI</p>	$\geq 60 \text{ cc}$
EROA (Effective Regurgitation Orifice Area)	<p>VOLUMETRIC METHOD</p> <p>EROA = Regurgitant volume / MR VTI</p> <p>PISA</p> <p>EROA = $6.28 \times \text{PISA radius}^2 \times \text{"aliasing" velocity} / \text{peak MR velocity}$</p> <div>  <ul style="list-style-type: none"> PISA corresponds to the time of peak MR velocity "Aliasing" velocity adjusted to the direction of regurgitation to obtain hemispheric convergence flow (Nyquist 20-40 cm/s) </div>	$\geq 0.40 \text{ cm}^2$ $(\geq 0.20 \text{ cm}^2 \text{ if functional MR})$
Regurgitant fraction	Regurgitant fraction = Regurgitant volume / $(0.785 \times \text{Mitral annulus diameter}^2 \times \text{antegrade mitral VTI})$	$\geq 50 \%$
PISA radius	Nyquist 40 cm/s	$\geq 9 \text{ mm}$
MR jet	<ul style="list-style-type: none"> Nyquist 50-60 cm/s Severe MR: Large central jet $> 10 \text{ cm}^2$ (or $> 40\%$ LA area) or eccentric jet adhering to the wall of the LA (Coanda effect) 	

E wave	Dominant E wave	> 1.2 m/s
Envelope of the jet on continuous Doppler	<ul style="list-style-type: none">• Severe MR: dense envelope; early peak and triangular shape• MVP: mid- or end-systolic envelope	
Pulmonary venous flow	Severe MR : systolic reversal	
LA dilatation and LV dilatation; Carpentier's mechanism		

AORTIC REGURGITATION		SEVERE
Vena contracta	Narrowest portion of the jet distal to the regurgitating orifice; PLAX; Nyquist 50-60 cm/s	≥ 6 mm
Regurgitant volume	<p>VOLUMETRIC METHOD</p> <p>Regurgitant volume = (0.785 x LVOT diameter² x LVOT VTI) - (0.785 x Mitral annulus diameter² + anterograde mitral VTI)</p> <ul style="list-style-type: none">• Mitral annulus diameter: mean of PLAX and AP4C• Significant MR: use pulmonic valve flow <p>PISA: Regurgitant volume = EROA x AR VTI</p>	≥ 60 cc
EROA (effective regurgitation orifice area)	<p>VOLUMETRIC METHOD</p> <p>EROA = Regurgitant volume / AR VTI</p> <p>PISA</p> <p>EROA = 6.28 x PISA radius² x “aliasing” velocity / peak AR velocity</p>	≥ 0.3 cm ²
Regurgitant fraction	<p>Regurgitant fraction =</p> <p>Regurgitant volume / (0.785 x LVOT diameter² x LVOT VTI)</p>	≥ 50 %
Jet width / LVOT diameter	PLAX; 1 cm inside the Ao valve; Nyquist 50-60 cm/s	≥ 65 %
Jet area / LVOT area	PSAX	≥ 60 %
Pressure half-time	<ul style="list-style-type: none">• Continuous Doppler• End-diastolic speed > 4 m/s• ↘ PHT: HTN; ↘ LV compliance; ↗ LVEDP	< 200 ms
Envelope of the jet on continuous Doppler	Severe AR : dense envelope (compare with density of the anterograde flow); rapid deceleration	
Holodiastolic flow reversal in descending aorta	<ul style="list-style-type: none">• Pulsed Doppler (after the origin of the L subclavian)• Also look for reversed flow in abdominal aorta• Reversal VTI ≈ anterograde flow VTI 	
LV dilatation; Ao dilatation; look for eversion or malcoaptation of leaflets; severe acute AR → restrictive mitral filling pattern		

PROSTHETIC VALVE

LOOK FOR: normal 60° opening of leaflets (normal movement of acoustic shadows); dehiscence / rocking movement; vegetation; thrombus; pannus; structural degeneration; abscess; intracardiac mass; pseudoaneurysm; fistula; periprosthetic regurgitation

- **Thrombus:** large mass; similar density to that of myocardium; recent symptoms; recent subtherapeutic INR; more frequent on mechanical mitral valve prosthesis
- **Pannus:** small, dense mass; not visualized in 30% of cases; more frequent in aortic valve prostheses

PROSTHETIC VALVE HEMODYNAMIC MEASUREMENTS: vary according to the model and dimensions of the prosthesis (compare with manufacturer's data); vary according to cardiac output

RECOVERY PRESSURE PHENOMENON: Ao transprosthetic gradient overestimated on TTE compared to catheterization (especially if proximal aortic diameter < 30 mm and small prosthesis)

PROSTHETIC REGURGITATION: distinguish physiological regurgitation specific to the prosthesis from pathological regurgitation; metallic mitral valve can hide MR due to shadowing

- **Central pathological regurgitation:** immobility of a mechanical leaflet; prolapse or perforation of a biological leaflet; mass - vegetation - thrombus
- **Periprosthetic pathological regurgitation:** dehiscence; rocking movement

PATIENT-PROSTHESIS MISMATCH: area of the effective prosthetic orifice too small for the patient's body surface area; **valve functions normally but with ↗ transvalvular gradients; normal prosthetic area (non-indexed) for the type of prosthesis** +

- **Mild:** Indexed EOA > 0.85 cm²/m²
- **Moderate:** Indexed EOA: 0.65-0.85 cm²/m²
- **Severe:** Indexed EOA < 0.65 cm²/m²; associated with ↗ mortality (especially if LV dysfunction)
- **Mitral prosthesis:** aim for indexed EOA > 1.2 cm²/m²

	PROSTHETIC AORTIC VALVE DYSFUNCTION			
	PEAK VELOCITY	VTI 1/2 RATIO	ACCELERATION TIME (AORTIC SYSTOLIC FLOW)	
Obstruction (degeneration; thrombus; pannus)	> 3 m/s	< 0.25	> 100 ms Delayed and parabolic peak	
Regurgitation or ↗ cardiac output	> 3 m/s	Normal (≥ 0.25)	AT < 80 ms Early triangular peak	
Patient-prosthesis mismatch	Indexed EOA < 0.85 cm²/m²			
	> 3 m/s	≥ 0.25	AT < 80 ms	
	PROSTHETIC MITRAL VALVE DYSFUNCTION			
	PEAK VELOCITY	GRADIENT	PHT	PROSTHETIC MITRAL VALVE VTI / LVOT VTI RATIO
Obstruction (degeneration; thrombus; pannus)	≥ 1.9 m/s	> 5 mmHg	> 130 ms	> 2.2
Regurgitation	≥ 1.9 m/s	> 5 mmHg	< 130 ms	> 2.2
Hyperdynamic state / High output state	≥ 1.9 m/s	> 5 mmHg	< 130 ms	< 2.2 (normal)

ECHOCARDIOGRAPHIC MASS

MASSES / STRUCTURES: Eustachian valve / crista terminalis bridge / Chiari network (RA); vegetation; thrombus; degenerative valve disease; calcification; pacemaker lead; central catheter; lipomatous interatrial septum; pericardial cyst; hydatid cyst; hiatal hernia; tuberculoma; Lambi's excrescences / valvular strands (filiform structures; length 3-10 mm; atrial aspect of AV valves and ventricular aspect of semilunar valves; on the line of leaflet closure); benign or malignant cardiac tumor (or metastasis)

THROMBUS: absence of opacification with contrast; adherent to a hypokinetic or akinetic region

CONTRAST ECHOCARDIOGRAPHY

AGITATED SALINE: 10 mL of saline solution; 0.25 mL of air emulsified with 2 syringes; right heart imaging

- **Intracardiac shunt:** opacification of L chambers within 3 beats (\pm Valsalva) +
- **Intrapulmonary shunt (AVMs):** opacification of L chambers after 5 beats +
- **Persistent left SVC:** injection into left arm \rightarrow opacification of coronary sinus

MICROBUBBLES: lipid microspheres containing gas and able to cross the pulmonary circulation allowing visualization of left cardiac structures; useful for LVEF - segmental wall motion - stress echocardiography - L chamber mass / thrombus (no enhancement in the presence of thrombus) - aneurysm / pseudoaneurysm - HCM - LV noncompaction

- **Complications:** 0.01 %
- **Contraindications:** perflutren allergy; significant PHT; R \rightarrow L shunt
- **Microbubbles mode:** reduction of mechanical index (0.4-0.5)

TISSUE AND STRAIN DOPPLER

TISSUE DOPPLER IMAGING (TDI): evaluates the velocity of longitudinal movement of a cardiac structure (low velocities); angle dependant

STRAIN (%): longitudinal deformation evaluation; percentage change in length of the muscle during contraction (negative value by convention) or relaxation (positive value by convention)

STRAIN RATE: instantaneous measurement of the deformation (contraction or relaxation)

TISSUE TRACKING: distance covered (displacement) by a structure over a given time interval

TISSUE DOPPLER (S WAVE) (CM/S)	SYSTOLIC STRAIN (%)	STRAIN RATE (S ⁻¹)	TISSUE TRACKING (cm)
Normal basal septum: 5.97 \pm 1.14	Normal basal septum: -17.5 \pm 5.32	Normal basal septum: 0.99 \pm 0.49	Normal basal septum: 1.2 \pm 0.19

SPECKLE TRACKING: evaluation of the deformation of a structure; angle-independent, which allows measurement of longitudinal, radial or circumferential deformation (counterclockwise systolic movement of the apex and clockwise systolic movement of the base)

- **Global longitudinal strain (%)**: relative length change of the LV myocardium between end-diastole and end-systole (**normal peak GLS in the range of -20%**) +

1.5/ TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE)

EVALUATION: mitral valve; aortic valve; prosthetic valve; endocarditis; LA; LAA - thrombus (pre-ECV); intracardiac mass; ASD; acute aortic syndrome; pulmonary venous return; perioperative; cardioembolic source; guidance of percutaneous procedures

COMPLICATIONS: < 1%; dental trauma; esophageal trauma; bronchospasm; laryngospasm; aspiration; respiratory depression; arrhythmias; methemoglobinemia (benzocaine)

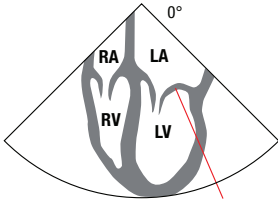
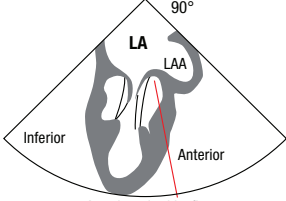
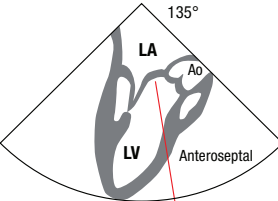
PREPARATION

- > **Contraindications:** dysphagia; esophageal disease; recent esophageal symptoms; esophageal varices; history of radiotherapy to the neck
- > **NPO:** minimum 6 hours before the examination (H₂O allowed until 2 hours before the examination)
- > Continuous ECG; IV route; O₂; saturation and BP monitor; suction
 - Resuscitation trolley at hand
- Flumazenil 0.2 mg IV PRN (benzodiazepine antagonist); Naloxone 0.1 to 0.4 mg IV PRN
- > **Anesthesia:** topical (lidocaine); IV sedation (midazolam 0.075 mg/kg, i.e. 2-4 mg; fentanyl PRN); Meperidine PRN (anti-gag; 25-50 mg IV)

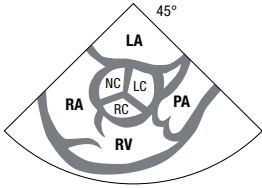
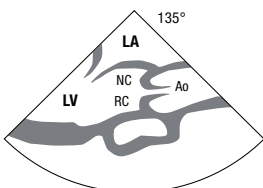
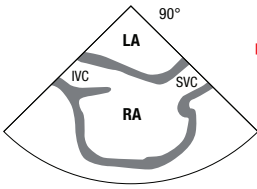
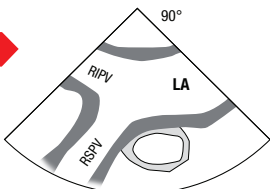
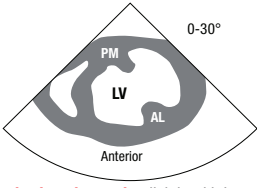
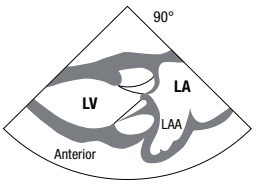
POST-EXAMINATION: NPO 2 hours post-examination; no driving for 12 hours

5 POSSIBLE MOVEMENTS

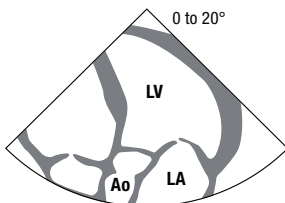
- 1) Advance - withdraw the probe
- 2) Rotation of the plane of section (0 degree = horizontal; 90 degrees = vertical)
- 3) Rotation of the hand piece: clockwise (R heart) or counterclockwise (L heart)
- 4) Antelexion (bending of the tip of the probe toward the sternum) or retroflexion
- 5) Lateral flexion to the right or left (rarely used)

INFERIOR TRANSESOPHAGEAL (30–35 CM)	
4 CHAMBERS - 0°	2 CHAMBERS - 90°
 <p>Posterior mitral leaflet</p>	 <p>Anterior mitral leaflet</p>
LONG AXIS - 135°	LEFT ATRIAL APPENDAGE
 <p>Anterior mitral leaflet</p>	<ul style="list-style-type: none"> • 45° on mitral valve: LAA to the right on the screen <ul style="list-style-type: none"> > Progressive rotation of the plane to evaluate the LAA (± slight withdrawal of the probe) • Rule out intra-LAA thrombus (circumscribed mass; bright; uniform texture and different from that of the LA wall) • Intra-appendicular velocities (Pulsed Doppler): < 20 cm/s associated with a risk of thromboembolic events • Look for spontaneous echo contrast (prothrombotic state)

+

SUPERIOR TRANSESOPHAGEAL	
SHORT AXIS (AORTIC VALVE) - 45°	LONG AXIS - 135°
 <ul style="list-style-type: none"> • Coronary ostia: 2 o'clock (left) and 6 o'clock (right) • Pulmonary valve and PA: 100-130° ± counterclockwise rotation 	 <ul style="list-style-type: none"> • NC = Non-coronary aortic leaflet • RC = Right coronary aortic leaflet
BICAVAL VIEW - 90°	PULMONARY VEINS - 90°
 <ul style="list-style-type: none"> • Clockwise rotation of the hand piece • Longitudinal interatrial septum • Rule out shunt: Color Doppler (Nyquist 30-40 cm/s); agitated saline (± Valsalva) • Pacemaker lead; central catheter 	 <ul style="list-style-type: none"> • On the bicaval view → clockwise rotation of the hand piece • Counterclockwise rotation of the hand piece: left pulmonary veins (adjacent to the LAA)
LEFT PULMONARY VEINS	
<ul style="list-style-type: none"> • LSPV: position the probe over the LAA (next to LSPV); slight withdrawal of the probe + antelexion + counterclockwise rotation of the hand piece (± rotation of the plane) • LIPV: after having localized the LSPV, look for the LIPV by counterclockwise rotation of the hand piece and/or progressive rotation of the plane 	
TRANSGASTRIC	
SHORT-AXIS LV (MITRAL PAPILLARY MUSCLES) 0-30°	2 CHAMBERS - 90°
 <p>Mitral valve, short axis: slightly withdraw the probe + slight antelexion + 10-20°</p>	 <p>110-135°: long axis (LVOT - Ao valve)</p>

5 CHAMBERS (DEEP TRANSGASTRIC) - 0 to 20°



- Maximum ante flexion
- Evaluation of LVOT

DESCENDING THORACIC AORTA

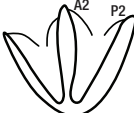

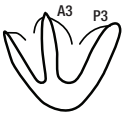
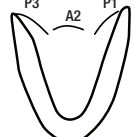
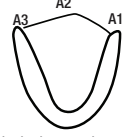

- Counterclockwise rotation of the hand piece
- 0°: short axis; 90°: long axis
- **Complex atherosclerosis**: plaque thickness ≥ 4 mm or mobile / pedunculated debris (= thrombus) or ulceration

MITRAL REGURGITATION - NATIVE VALVE

MECHANISM: Carpentier classification (►► Chapter 4 - Valvular heart disease); prolapse; eversion; restriction; annular dilatation; perforation

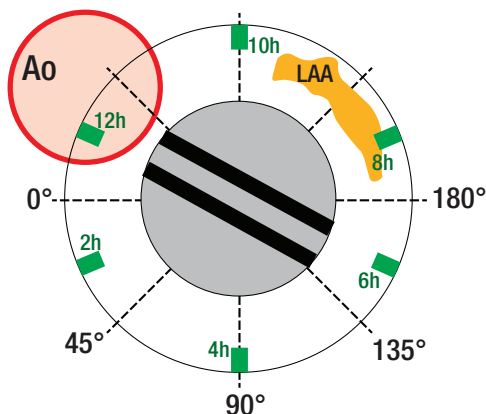
IDENTIFICATION OF THE SEGMENTS INVOLVED

- > **A1-P1**: anterolateral
- > **A3-P3**: posteromedial

STEP 1	 <p>Baseline image</p>	 <p>Ante flexion or withdrawal of the probe</p>	 <p>Probe advanced or retro flexion</p>
STEP 2	 <p>Baseline image</p>	 <p>Clockwise rotation of hand piece</p>	 <p>Counterclockwise rotation of hand piece</p>

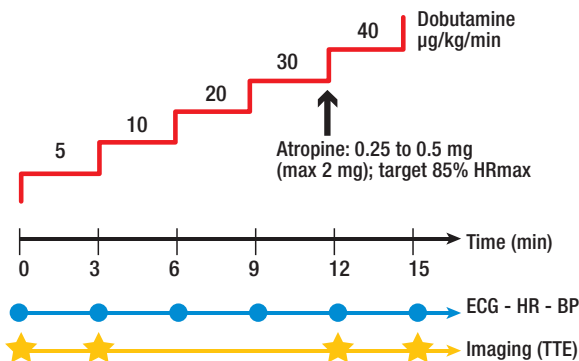
MITRAL REGURGITATION - PROSTHETIC VALVE

IDENTIFICATION OF THE SURGICAL QUADRANT: transesophageal 4 chambers (0°); rotation of the plane of section every 10° for 180°



1.6/ STRESS ECHOCARDIOGRAPHY

STRESS: exercise (Bruce protocol) or Dobutamine



INDICATIONS TO STOP DOBUTAMINE STRESS ECHOCARDIOGRAPHY: > 85 % HRmax predicted for age; moderate *de novo* (or progressive) RWMA; significant arrhythmia; hypotension; severe HTN; intolerable symptoms

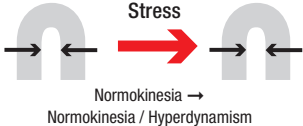
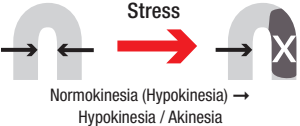
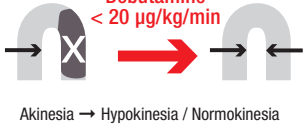

> **Antidote to dobutamine:** beta-blocker

COMPLICATIONS (DOBUTAMINE): angina; hypotension; VT (4%); supraventricular tachyarrhythmia / AF; VF or myocardial infarction (1 / 2,000 studies)

CONTRAST AGENT: ≥ 2 segments poorly visualized on baseline TTE

STRESS-INDUCED ISCHEMIA

- a) **RWMA (regional wall motion abnormality):** deterioration ≥ 1 grade of segmental wall motion (normokinetic or hypokinetic segment at rest); deterioration of endocardial excursion and/or segmental thickening
- b) **Tardikinesia:** delayed and slow segmental contraction
- c) **Chamber dilatation:** \nearrow end-systolic LV volume
- d) \searrow **LVEF:** deterioration of global systolic function

NORMAL RESPONSE	ISCHEMIA
 <p>Normokinesia \rightarrow Normokinesia / Hyperdynamism</p>	 <p>Normokinesia (Hypokinesia) \rightarrow Hypokinesia / Akinesia</p>
VIABILITY (HIBERNATION)	SCAR (NECROSIS)
 <p>Dobutamine $< 20 \mu\text{g/kg/min}$</p> <p>Akinesia \rightarrow Hypokinesia / Normokinesia</p>	 <p>Stress</p> <p>Akinesia (Dyskinesia) \rightarrow Akinesia (Dyskinesia)</p>

SCAR: regional wall motion abnormality unchanged by stress test (fixed deficit); thin < 6 mm and echodense (fibrotic) segment

DECREASED PREDICTIVE VALUE: target HR not achieved; LVH / concentric remodeling; imaging > 60 s post-stress; 1-vessel disease (particularly circumflex); LBBB; ventricular pacing

FINDINGS IN REPORT: type of stress protocol; result of stress test or dose of dobutamine used; maximum HR reached; test validity ($> 85\%$ HRmax); BP; reason for interruption; symptoms on stress test; ECG abnormalities; arrhythmias; ischemic threshold; segmental wall motion at rest and on stress test; LVEF and end-systolic LV volume at rest and on stress test

FACTORS OF POOR PROGNOSIS

- \triangleright **Resting LVEF:** $< 35\%$
- \triangleright **Low ischemic threshold:** dobutamine $\leq 10 \mu\text{g/kg/min}$ or $< 70\%$ HRmax predicted or HR < 120 bpm
- \triangleright **WMSI on effort:** > 1.4 to 1.7
- \triangleright **Extensive ischemia:** ≥ 3 segments
- \triangleright **Ischemia in several coronary territories (≥ 2 vessels)**
- \triangleright **Deterioration of LVEF ($< 45\%$ or \searrow LVEF $\geq 10\%$) or LV dilatation on stress test**

NEGATIVE STRESS ECHOCARDIOGRAPHY: annual risk of cardiac event $< 1\%$ (exercise) or $< 2\%$ (dobutamine)

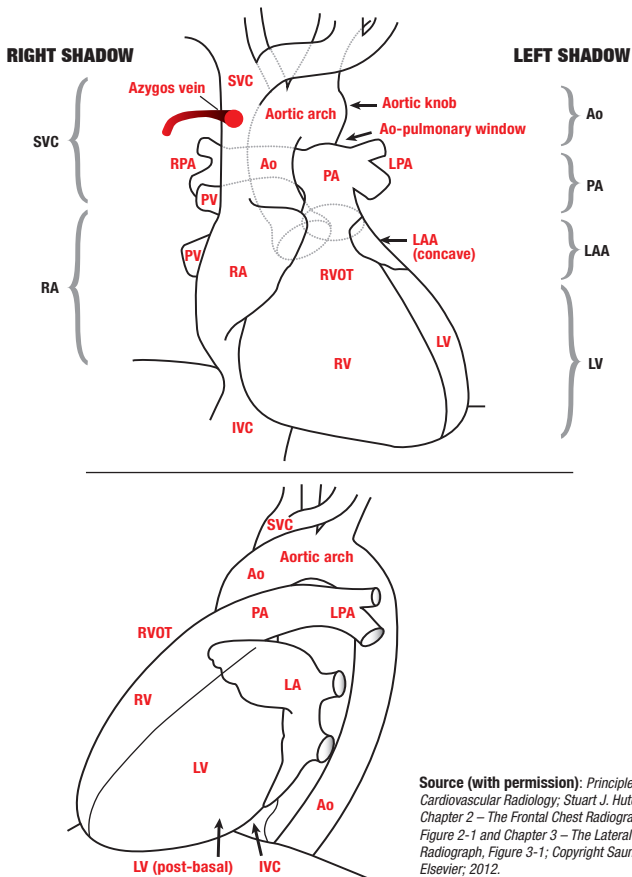
VIABILITY: improvement of the segmental wall motion (≥ 1 grade $\times \geq 2$ segments) with low-dose dobutamine ($2.5 - 5 - 7.5 - 10 - 20 \mu\text{g/kg/min}$)

- \triangleright **Biphasic response:** improvement of wall motion at low-dose then deterioration at higher dose (up to $40 \mu\text{g/kg/min}$); specific for improvement of wall motion post-revascularization
- \triangleright **Sustained improvement:** viable but non-ischemic segment

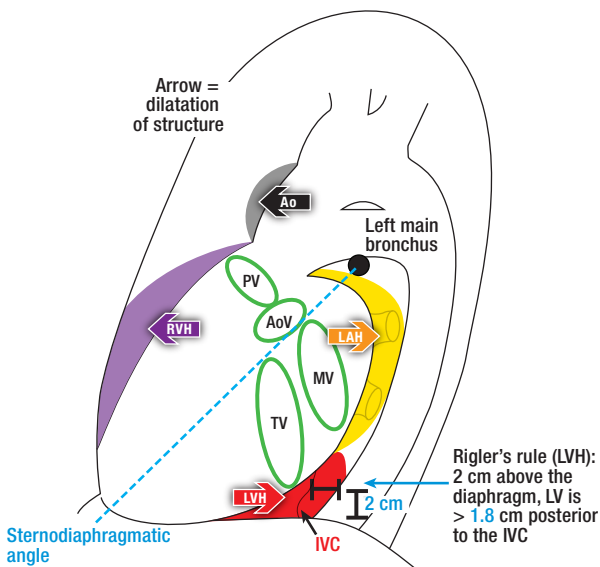
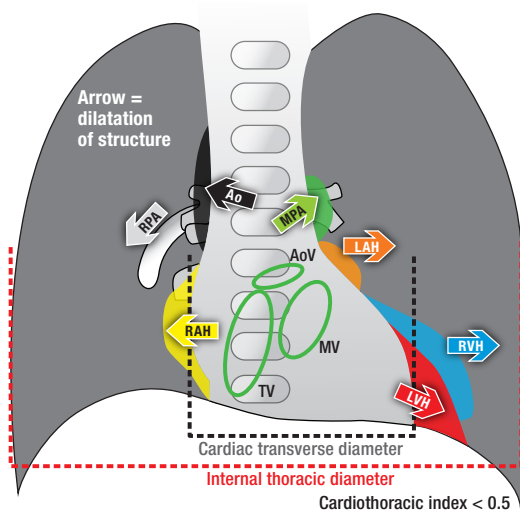
1.7/ CHEST X-RAY

QUALITY CONTROL: **A)** Patient - Date; **B)** Adequate inspiration (right hemidiaphragm below the 6th rib anteriorly and below the 10th rib posteriorly); **C)** Patient centered - Absence of rotation (tracheal air column in the center of the vertebral bodies; spinous processes of vertebral bodies centered between clavicles); **D)** Adequate penetration (spinous processes of thoracic vertebral bodies visible); **E)** Compare with previous films

SYSTEMATIC APPROACH: Situs (gastric bubble and apex); Cardiothoracic index; Heart shadow and cardiac structures (RA; LA; RV; LV; Ao; PA); Calcifications; Pulmonary venous and arterial blood supply; Hila; Lung parenchyma; Pleura; Bone structures; Prosthetic material



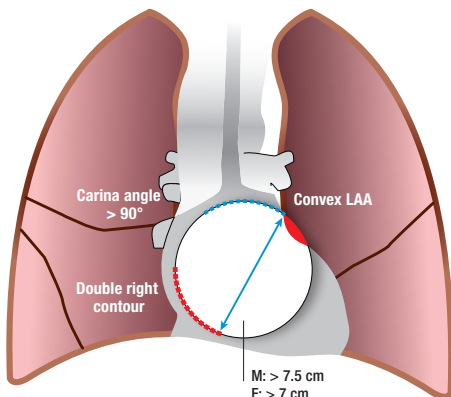
Source (with permission): *Principles of Cardiovascular Radiology*; Stuart J. Hutchison; Chapter 2 – The Frontal Chest Radiograph, Figure 2-1 and Chapter 3 – The Lateral Chest Radiograph, Figure 3-1; Copyright Saunders Elsevier; 2012.



CARDIOTHORACIC INDEX (PA): < 0.5

- > **False-positive:** AP film; Obesity; Pregnancy; Pectus excavatum; Ascites; Scoliosis; Under-inspiration

LA DILATATION: convexity of the LAA (between LPA and LV); quadruple contour (Ao; PA; LAA; LV); elevation of left main bronchus (carina angle > 90°); right double contour; posterior dilatation on lateral film



RA DILATATION: right shadow shifted towards the right; ± dilatation of SVC - IVC - azygos vein secondary to ↗ CVP

RV DILATATION: transverse displacement of the left shadow; **RV > 1/3 of the distance between the cardiophrenic angle and the sternal angle (lateral film);** ± PA dilatation

- > **DDx of filling of retrosternal space:** post-sternotomy; lymphadenopathy; mediastinal mass (lymphoma; thymoma; thyroid); pulmonary trunk dilatation; aortic root dilatation; small antero-posterior diameter (pectus excavatum; scoliosis; kyphosis)

LV DILATATION: prominent apex displaced downwards; downward displacement of gastric bubble and posterior displacement of LV (> 1.8 cm with respect to IVC) on the lateral film

PA DILATATION: L → R shunt; post-stenotic dilatation (main PA and LPA); Pulmonary hypertension (venous or arterial); PR; idiopathic

- > **RPA dilatation:** > 17 mm

- > **Main PA dilatation:** prominence between the aortic knob and the LAA

ASCENDING AORTA DILATATION: prominent right contour of mediastinum; prominent anterior contour of mediastinum on lateral film; distance between left lateral edge of tracheal air column and aortic knob > 35 mm

NORMAL PULMONARY BLOOD SUPPLY: peripheral attenuation (distal 1/3 not visible); vessels at base > vessels at lung apex

- > **Venous congestion (venous PHT):** redistribution to apices (cephalization); blurred peripheral vessels; Kerley B lines (1-3 cm long; 1 mm thick; horizontal; arising from pleura); interstitial edema; peribronchial edema; prominent and blurred hila; edema of fissure; pleural effusions; alveolar edema; PA dilatation
- **Dilatation of azygos vein (>1 cm):** Right heart failure (↗ CVP); SVC obstruction; Constrictive pericarditis; IVC interruption (venous return via azygos system); anomalous PV connection

- > **Peripheral hypervascularization** (vessels visible below the diaphragm)
 - a) **L→R shunt**: Dilated PA; branches of PA > associated bronchi; dilatation of heart chambers
 - b) **High output state**: pregnancy; hyperthyroidism; anemia
- > **Peripheral hypovascularization**
 - a) **PHT**: RVH; PA - LPA - RPA dilatation; **early and marked attenuation of peripheral vessels**
 - b) **RVOT obstruction**: post-stenotic LPA dilatation in the presence of PS; RVH

1.8/ CORONARY ANGIOGRAPHY

PREPARATION

BASIC WORK-UP: CBC; ECG; electrolytes; creatinine-BUN; Clotting tests; target INR < 2.0

DIABETES: Discontinue metformin in the event of post-coronary angiography ARF

PREVENTION OF CONTRAST NEPHROPATHY: particularly if GFR < 60 mL/min or DM

- a) **Hydration with normal saline**: 1 mL/kg/h x 3-12 h before and 6-24 h after angiography (0.5 mL/kg/h if LVEF < 35% or NYHA III-IV)
- b) **Minimize the volume of contrast**: < 300 mL or < 4 mL/kg; avoid a contrast volume (mL) / GFR ratio > 3.7; avoid multiple procedures < 48-72 h
- c) **No benefit of N-acetyl-L-cysteine** (★ACT)
- d) **Avoid nephrotoxic medications** (NSAIDs; ACE inhibitors; ARB)
- e) **Preferred contrast agents**: **nonionic** (iso-osmolar or low osmolar)

IODINE ALLERGY: Prednisone 50 mg 12 h and 1 h before coronary angiography; Diphenhydramine 50 mg PO and Ranitidine 150 mg PO 1 h before coronary angiography

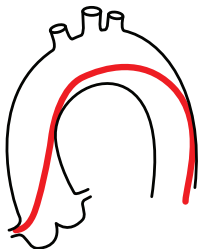
> **Urgent coronary angiography**: Methylprednisolone 125 mg IV + Diphenhydramine 50 mg

VASCULAR ACCESS

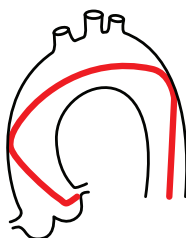
FEMORAL ACCESS: use the common femoral artery; puncture site 3 cm below the inguinal ligament (anterior superior iliac crest to superior pubic ramus) but proximal to the femoral bifurcation (bifurcation distal to the middle third of the femoral head); risk of retroperitoneal bleeding if the artery is punctured too high; risk of pseudoaneurysm if the artery is punctured too low

> **Withdrawal of the introducer**: ACT < 180 s

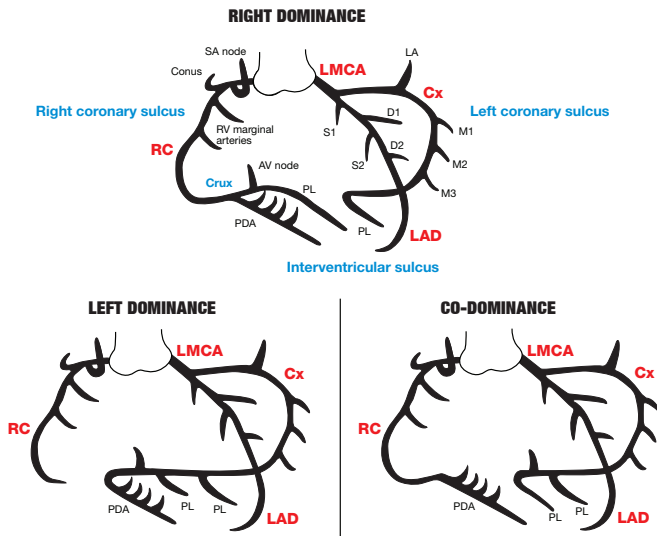
RADIAL ACCESS: Allen's test before (color returns to normal < 10 seconds); intraarterial Verapamil; Heparin IV (bolus of 2000 to 5000 units); 4-6 F catheters (1 F = 0.3 mm)



Right Judkins Catheter in the RCA



Left Judkins Catheter in the LCA



Source (with permission): CathSource iPad application; Rocky Bilhartz, MD; <http://ecgsources.com>

RIGHT DOMINANCE: 85% of patients; **PDA + ≥ 1 PL arise from the RCA**

- > **Left dominance:** 7%; PDA and ≥ 1 PL arise from the circumflex; small RCA that does not perfuse the LV wall (ends before the crux cordis)
- > **Co-dominance:** 7%; PDA arises from the RCA; all PL arise from the circumflex

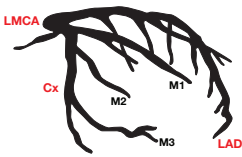
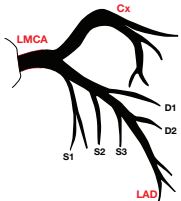
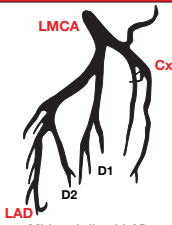
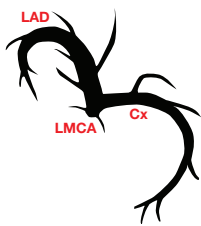
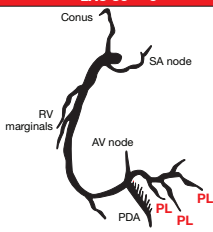
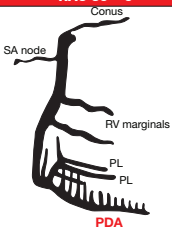
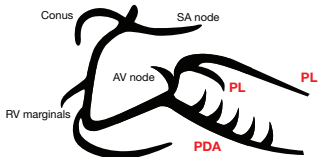
VEIN GRAFT: adjacent to surgical clip

- a) **Bypass graft of the RCA:** 5 cm above the sinotubular junction; right anterolateral aspect of the Ao
- b) **Bypass graft of the LAD:** 7 cm above the sinotubular junction; anterior aspect of the Ao
- c) **Bypass graft of the circumflex:** 9 cm above the sinotubular junction; left anterolateral aspect of the Ao

ANGIOGRAPHIC VIEWS

OBTAIN AT LEAST 2 PERPENDICULAR VIEWS for each vessel (to exclude eccentric lesions)

- 1) **RAO versus LAO versus PA versus lateral**
- 2) **Cephalic versus Caudal** (depending on the direction towards which the image intensifier above the patient is inclined); cephalic view \rightarrow circumflex superior on the image; caudal view \rightarrow LAD superior on the image

LEFT CORONARY	
RAO 30° - CAUDAL 25°	RAO 10° - CEPHALIC 40°
 <p>Cx - Marginals - Distal LAD</p>	 <p>LAD - Septal - Diagonals</p>
LAO 45° - CEPHALIC 25°	SPIDER: LAO 45° - CAUDAL 45°
 <p>Mid and distal LAD - Diagonals - Distal dominant Cx</p>	 <p>LMCA - Proximal LAD - Proximal Cx</p>
RIGHT CORONARY	
LAO 30° - 0°	RAO 30° - 0°
 <p>Proximal and mid RCA; PLs</p>	 <p>Mid RCA / Mid PDA</p>
PA - 20° CEPHALIC	
 <p>Distal RCA: PDA and PLs</p>	

Redrawn and expanded from (with permission): Uptodate 2015; Zimetbaum P.J, Josephson M.E. Conduction abnormalities after myocardial infarction; www.uptodate.com; Post TW (Ed). UpToDate, Waltham, MA, March 2015.

CORONARY ARTERY STENOSIS

ANGIOGRAPHIC	HEMODYNAMIC	IVUS (INTRAVASCULAR ULTRASOUND)
$\geq 70\%$ (LMCA: $\geq 50\%$)	$FFR \leq 0.80$	• LMCA: Area $< 6 \text{ mm}^2$ (6 to $7.5 \text{ mm}^2 \rightarrow$ determine FFR) • Other vessels: Area $< 4 \text{ mm}^2$

CHARACTERISTICS OF THE CORONARY LESION		
TYPE A: PCI WITH HIGH SUCCESS RATE ($> 85\%$) AND LOW RISK	TYPE B: PCI WITH MODERATE SUCCESS RATE (60-85%) AND MODERATE RISK	TYPE C: PCI WITH LOW SUCCESS RATE ($< 60\%$) AND HIGH RISK
<ul style="list-style-type: none"> • Short (10 mm) • Concentric • Only slightly calcified • Not totally occluded • Not ostial • Easily accessible • Not angulated ($< 45^\circ$) • Regular contours • No branch lesion • Absence of thrombus 	<ul style="list-style-type: none"> • Tubular (10-20 mm) • Eccentric • Moderately calcified • Total occlusion < 3 months • Ostial • Moderate tortuosities of proximal segment • Moderate angulation ($45-90^\circ$) • Irregular contours • Bifurcation • Presence of thrombus 	<ul style="list-style-type: none"> • Diffuse (> 20 mm) • Severe tortuosities of proximal segment • Extreme angulation ($> 90^\circ$) • Bifurcation with impossibility to protect a major branch • Vein graft with friable lesions

- a) **Length:** short (< 10 mm) - tubular (10-20 mm) - diffuse (> 20 mm)
 b) **Ostial:** < 3 mm from the ostium; aorto-ostial stenosis often fibrocalcified
 c) **Bifurcation:** Medina's X, Y, Z classification
 > **X:** 0 if absence of stenosis or 1 if stenosis in the main proximal segment
 > **Y:** 0 if absence of stenosis or 1 if stenosis in the main distal segment
 > **Z:** 0 if absence of stenosis or 1 if stenosis in the daughter branch
 d) **Calcification:** confers rigidity and non-compliance to the dilatation
 e) **Angulation:** $> 45^\circ$ moderate; $> 90^\circ$ severe; makes stent placement more difficult and associated with a risk of late stent fracture
 f) **Thrombus:** risk of distal microembolism
 g) **Eccentricity:** variable stenosis according to angiographic view
 h) **Irregularities:** ulcer; intimal flap; aneurysm; saw tooth irregularities (multiple successive irregular stenoses)
 i) **Tortuosity of the proximal segment:** moderate (2 proximal curves $> 75^\circ$) or severe (3 proximal curves $> 75^\circ$)
 j) **Presence of collaterals:** Rentrop classification
 k) **TIMI flow**

TIMI 0	Total occlusion
TIMI 1	Presence of a very faint antegrade flow beyond the stenosis; no opacification of the distal coronary bed
TIMI 2	Opacification of the entire distal coronary bed, but sluggish flow (compared to vessels with normal flow)
TIMI 3	Antegrade perfusion of all of the distal coronary bed; normal filling velocity

MICROVASCULAR EVALUATION: myocardial "blush" score

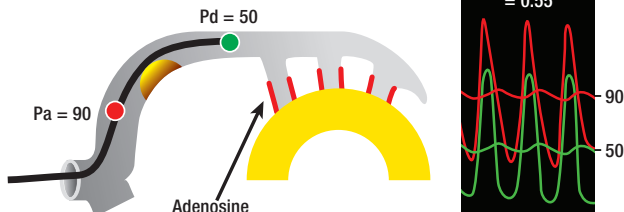
FRACTIONAL FLOW RESERVE (FFR)

INDICATION: estimate the hemodynamic impact of an intermediate angiographic stenosis (50-70%)

CALCULATION: Pressure distal to lesion (P_d) / Pressure proximal to lesion (P_a) ratio during maximum hyperemia (IV or intracoronary adenosine)

CORONARY BLOOD FLOW DEPENDS ON: **A)** DBP; **B)** Arteriolar resistance; **C)** Left intraventricular pressure; **D)** Degree of coronary stenosis

> **Abnormal FFR:** ≤ 0.80 (★ FAME; ★ FAME-2)

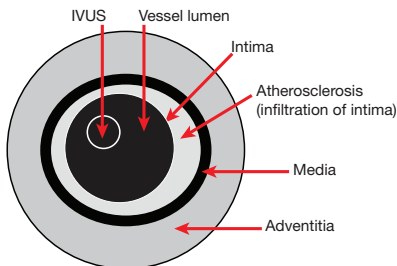


INTRAVASCULAR ULTRASOUND (IVUS)

Transverse ultrasound section of the lumen and arterial wall

EVALUATION: real dimensions of the lumen; abnormality of the arterial wall; degree of atherosclerotic infiltration; positive vascular remodeling (Glagov phenomenon)

INDICATION: **A)** Specify the severity of LMCA stenosis; **B)** Complex lesion (ostial; bifurcation; aneurysm; dissection); **C)** Bypass graft disease; **D)** Restenosis or intra-stent thrombosis; **E)** Guidance during PCI / evaluation of stent deployment



COMPLICATIONS

COMPLICATIONS: Major complications < 1%; Death; MI; Contrast nephropathy; Stroke; Local vascular complication (thrombosis; distal embolism; dissection; hematoma; pseudoaneurysm; AV fistula); Arrhythmia; Allergy; Air embolism; Coronary artery dissection; Atheroembolism

ANAPHYLAXIS: epinephrine 1:10,000 - **1 mL IV every minute (0.1 mg every minute)** +

HEPARIN ANTIDOTE: Protamine (1 mg for every 100 units of heparin; if IV infusion of heparin → 25-50 mg of protamine IV slowly); risk of allergy if the patient is treated with NPH insulin

➤ www.medicines.org.uk/emc/medicine/10807/spc

RETROPERITONEAL HEMATOMA: secondary to puncture above the inguinal ligament; hypotension / abdominal pain / back pain; CBC - clotting tests; CT scan; reverse anticoagulation; transfusion PRN; medical treatment in the majority of cases (or covered stent)

PSEUDOANEURYSM: pulsatile mass with systolic murmur; ultrasound diagnosis; good prognosis if diameter < 2 cm

- **Noninvasive percutaneous treatment:** ultrasound-guided compression or local injection of thrombin; follow-up US at 1 month
- **Surgery:** large or rapidly progressive pseudoaneurysm or infected or failure of noninvasive treatment

AV FISTULA: secondary to puncture below the femoral bifurcation; thrill or continuous murmur; surgical treatment in the majority of cases (risk of progression)

RADIAL ACCESS COMPLICATIONS: Hematoma; Arterial dissection or occlusion; Loss of radial pulse; Compartment syndrome; Spasm

POST-CORONARY ANGIOGRAPHY ARF

- **Contrast nephropathy:** Early and reversible ARF; Improvement by day 3 to 5

RISK OF CONTRAST NEPHROTOXICITY POST-PCI		
Hypotension	5 points	≤ 5 POINTS
IABP	5 points	
Heart failure	5 points	6-10 POINTS
> 75 years	4 points	
Anemia	3 points	11-16 POINTS
Diabetes	3 points	
Each 100 mL of contrast	1 point	> 16 POINTS
Creatinine > 130 mmol/L or	4 points or	
GFR 40-60 mL/m ²	2 points	
GFR 20-40 mL/m ²	4 points	
GFR < 20 mL/m ²	6 points	

Mehran R, Aymong ED, Nikolsky E et al. JACC 2004; 44; 1393-1399.

- **Atheroembolism:** subacute ARF (several days to several weeks); **eosinophilia / eosinophiluria; slightly active urinary sediment; hypocomplementemia; other micro atheroembolic lesions** (toes; livedo reticularis; petechiae; splinter hemorrhage; mesenteric or pancreatic ischemia; retinal Hollenhorst plaques); slight improvement of renal function

1.9/ HEMODYNAMIC ASSESSMENT

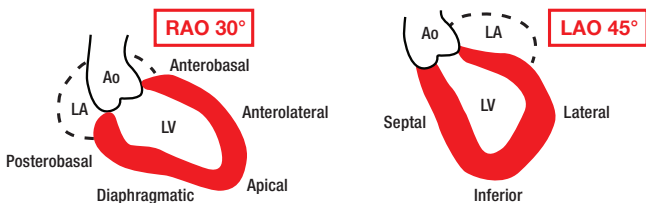
INDICATIONS: More refined assessment of heart disease when noninvasive evaluation is insufficient (heart failure; valvular heart disease; PHT; complicated myocardial infarction; congenital heart disease; intracardiac shunt; pericardial disease; cardiomyopathy; biopsy)

COMPLICATIONS: < 1%; death; MI; stroke; arrhythmia; access site complication; allergy to contrast agent; cardiac tamponade / perforation; RBBB during catheterization of RV and LBBB during catheterization of LV; pulmonary infarction; PA perforation

RIGHT CARDIAC CATHETERIZATION: RA - RV - PA - pulmonary capillary wedge pressures; cardiac output; search for a shunt; calculation of pulmonary vascular resistance

LEFT CARDIAC CATHETERIZATION: LA pressure (transseptal or estimated by wedge pressure) - LV - Ao pressures; coronary angiography; left ventriculography and aortography; calculation of systemic vascular resistance; evaluation of valvular heart disease

- **Transseptal:** verification of the correct position (LA) by atrial pressure curve - oxygen saturation - contrast injection
- **Left ventriculography:** RAO 30° ± LAO 45° (30-40 mL of contrast)



HEMODYNAMIC DATA

MEASUREMENTS: at the end of expiration

+

	MEAN	NORMAL
Cardiac output (L/min)	5	4 - 6
Cardiac Index (L/min/m²)	3.5	2.5 - 4.5
Aorta pressure (mmHg)		
Systole	130	90-140
End-diastole	70	60-90
Mean	85	70-105
Mean BP = 1/3 x SBP + 2/3 X DBP		
LV PRESSURE (mmHg)		
Systole	130	90-140
End-diastole	8	5-12
LA pressure (v > a) (mmHg)		
Max	12	6-21
Mean	8	2-12
PCWP (mmHg)		
Mean	9	4-12
PAP (mmHg)		
Systole	25	15-30
End-diastole	9	4-12
Mean	15	9-19
Mean PAP = 1/3 x sPAP + 2/3 x dPAP		

	MEAN	NORMAL
RV pressure (mmHg)		
Systole	25	15-30
End-diastole	4	1-7
RA (a > v) (mmHg)		
Max	6	2-7
Mean	3	1-5
Resistance (dyn x s / cm⁵)		
Systemic vascular resistance	1100	700-1600
Pulmonary vascular resistance	70	20-130
<ul style="list-style-type: none"> • $\Delta P = Q \times R$ • Systemic vascular resistance (WU) = Mean arterial pressure - Mean RA pressure / Systemic output • Pulmonary vascular resistance (WU) = Mean PAP - Mean wedge pressure / Pulmonary output • Conversion: 1 WU = 80 dyn x s / cm⁵ 		

CARDIAC OUTPUT

FICK: gold standard method

- **Systemic cardiac output (L/min)** = O_2 consumption (mL/min) / $1.36 \times \text{Hb (g/L)} \times (\text{Aortic SaO}_2 - \text{Mixed venous SaO}_2)$
- **Pulmonary cardiac output (L/min)** = O_2 consumption (mL/min) / $1.36 \times \text{Hb (g/L)} \times (\text{PV SaO}_2 - \text{PA SaO}_2)$

- **Estimation of O_2 consumption:** 125 mL/m² in young subjects; 110 mL/m² in elderly subjects
- **SaO₂:** expressed as a decimal (70% = 0.70)
- **Mixed venous SaO₂:** = $3/4 \times \text{SVC SaO}_2 + 1/4 \times \text{IVC SaO}_2$
- **Caveats: A)** Estimation of VO_2 (instead of measurement of VO_2 by face tent); **B)** High output (attenuated arteriovenous O_2 difference)

THERMODILUTION: injection of a bolus of NaCl into the vena cava; detection of a change of temperature as a function of time in a distal port (pulmonary artery); **cardiac output is inversely proportional to the area under the curve**

- **Caveats: A)** Significant TR (underestimates cardiac output); **B)** Low output (< 2.5 L/m) in which case cardiac output is overestimated; **C)** Intracardiac shunt (cardiac output overestimated if $L \rightarrow R$ shunt)

ANGIOGRAPHIC METHOD

- **Cardiac output** = (LV end-diastolic volume - LV end-systolic volume) x HR

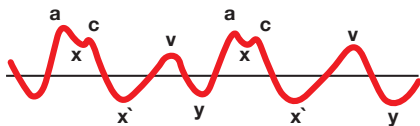
- **Caveats: A)** Evaluation of cardiac output in a single cardiac axis; **B)** Less reliable in the presence of MR, AR or AF

HEMODYNAMIC CURVES

Use the ECG to identify waves on the curves

- A) Polyphasic curves:** atrial recording; pulmonary capillary wedge pressure recording
- B) Monophasic curve**
 - **Ventricular recording:** End-diastolic pressure > Early diastolic pressure
 - **Arterial recording:** Early diastolic pressure > End-diastolic pressure

ATRIAL RECORDING



RA recording

A WAVE: atrial kick; **follows the P wave on the ECG**

- > **Normally:** $a > v$ in RA; $v > a$ in LA
- > **↗ a wave:** MS (or TS); **↘** ventricular compliance (LVH or RVH; LVOT or RVOT obstruction)
- > **Canon a wave:** AV dissociation (AV block; ventricular pacemaker; VT; PVC; PAC)
- > **Absent a wave:** AF or atrial flutter; severe atrial disease (Ebstein; rheumatic MS; cardiac amyloidosis)

X DESCENT: atrial relaxation; **after S1**

- > **↗ x descent:** Tamponade; Constriction (W-M pattern)

C WAVE: protrusion of the AV valve into the atrium during isovolumic contraction of the ventricle

X' DESCENT: atrial relaxation + descent of AV valve during systolic ejection

V WAVE: passive atrial filling during ventricular systole in the presence of a closed AV valve;
at the end of the T wave on the ECG

- > **↗ v wave:** MR (or TR); VSD (or ASD on RA recording); rheumatic MS (**↘** LA compliance); Heart failure

Y DESCENT: emptying of the atrium following opening of the AV valve (rapid ventricular filling);
after S2

- > **↗ y descent:** Constriction; RCM; MR (or TR)
- > **↘ y descent:** Tamponade; MS (or TS)

PCWP: pulmonary capillary wedge pressure; similar curve to LA but delayed by 40-120 ms (pressure transmission delay) and slightly attenuated

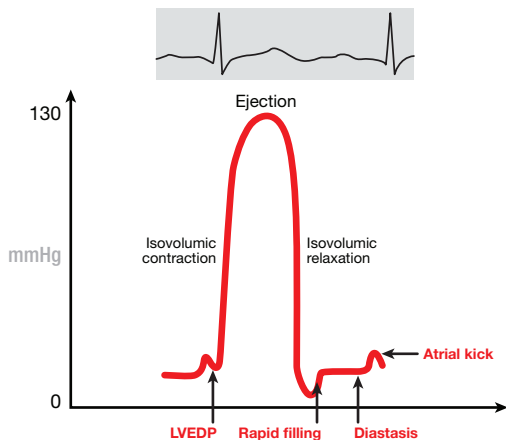
- > **Adequate wedge pressure:** oximetric confirmation ($\text{SaO}_2 > 95\%$); injection of contrast; respiratory variation of the curve
- > **Inequality between wedge pressure and LA pressure:** PV obstruction; **↗** Pleural pressure; Catheter in non-dependent pulmonary zone (target West zone 3)
- > **dPAP > Wedge:** Pulmonary disease; Pulmonary embolism; significant PHT

VENTRICULAR RECORDING

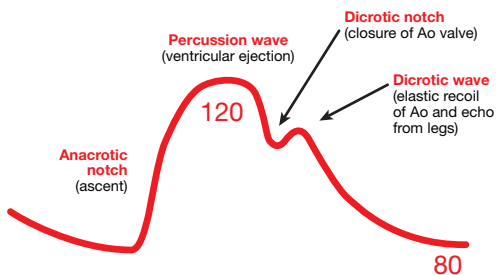
SYSTOLE: **A)** Isovolumic contraction; **B)** Ejection; **C)** Reduced ejection then start of relaxation

DIASTOLE: **A)** Isovolumic relaxation; **B)** Rapid filling; **C)** Slow filling (diastasis); **D)** Atrial kick

- > **End-diastolic pressure:** after atrial kick at point c (simultaneous with QRS)



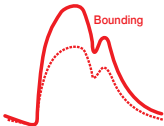
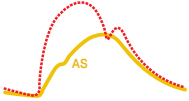
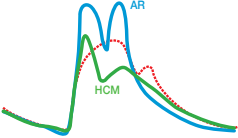
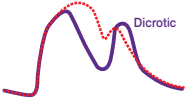
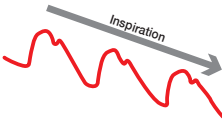
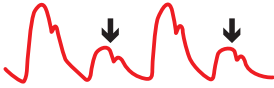
ARTERIAL RECORDING



PULSE PRESSURE: reflects the stroke volume and compliance of the arterial system

- > ↗ **pulse pressure:** **> 50 % of SBP** (or > 40 mmHg); HTN; Age; AR; patent ductus arteriosus; Ruptured aneurysm of the sinus of Valsalva; Fever; Anemia; Hyperthyroidism; Pregnancy; AV fistula; Paget's disease +
- > ↘ **pulse pressure:** **< 25% of SBP**; Tamponade; Heart failure; Cardiogenic shock; Aortic stenosis +

CAROTID PULSE: similar to central aortic pulsation

CORRIGAN'S PULSE (BOUNDED)	 <p>Bounding</p> <p>Abrupt systolic ascent, followed by rapid collapse; increased pulse pressure</p>	<p>DDx: AR; patent ductus arteriosus; truncus arteriosus; fever; anemia; hyperthyroidism; pregnancy; exercise; AV fistula; Paget's disease; Beriberi; bradycardia in an elderly patient with non-compliant aorta</p>
PULSUS PARVUS ET TARDUS (ANACROTIC)	 <p>AS</p>	<ul style="list-style-type: none"> • AS • Tardus: slow ascent • Parvus: decreased amplitude • \pm Thrill
PULSUS BISFERIENS (BIFID)	 <p>AR</p> <p>HCM</p> <p>2 peaks during systole (percussion wave then tidal wave)</p>	<ul style="list-style-type: none"> • DDx: AR; HCM; patent ductus arteriosus • Tidal wave: echo from leg vessels • HCM: spike and dome (rapid initial ascent then dynamic LVOT obstruction)
DICROTIC PULSE	 <p>Dicrotic</p> <p>1 peak in systole and 1 peak in diastole</p>	<p>DDx: IABP; severe heart failure; tamponade; hypovolemia; sepsis</p>
PULSUS PARADOXUS	 <p>Inspiration</p> <p>> 10 mmHg reduction of systolic blood pressure on inspiration</p>	<p>DDx: Tamponade; constriction - effusion; RCM; COPD; Asthma; Pulmonary embolism; Pneumothorax; Hypovolemia; Obesity; Pregnancy</p> <ul style="list-style-type: none"> • Reversed pulsus paradoxus: HCM
PULSUS ALTERNANS		<p>DDx: Severe heart failure; bigeminy; tamponade; severe AR; tachypnea</p>

AORTIC STENOSIS

TRANSVALVULAR GRADIENT: measurement of blood pressures in proximal Ao and LV

- **Mean gradient:** integral of the transvalvular gradient during systole
- **Peak-to-peak gradient:** not physiological as peaks not simultaneous
- **Pressure in femoral artery:** underestimation of transvalvular gradient (due to peripheral amplification of SBP)

FIXED OBSTRUCTION: *pulsus parvus et tardus* on aortic recording

CARABELLO'S SIGN: > 10 mmHg increase in SBP following withdrawal of the catheter from the LV towards the aorta (obstructive catheter in critical aortic stenosis)

HAKKI FORMULA: Aortic valve area = CO (L/min) / $\sqrt{\text{mean gradient (or peak-to-peak gradient)}}$

GORLIN FORMULA: Aortic valve area = Stroke volume (mL/beat) / (44.3 x Systolic ejection period (s / beat) x $\sqrt{\text{Mean gradient mmHg}}$)

CAVEATS: **A)** Concomitant AR: calculate cardiac output (or stroke volume) by the angiographic method; **B)** Aortic stenosis in the presence of low cardiac output (dobutamine challenge)

MITRAL STENOSIS

TRANSVALVULAR GRADIENT: transeptal measurement of LA and LV pressures

- **LA pressure estimated by PCWP:** overestimates the transvalvular gradient (delayed transmission of pressure waves and attenuation of y descent)

GORLIN FORMULA: Mitral valve area = Stroke volume (mL/beat) / (37.7 x Diastolic filling period (s / beat) x $\sqrt{\text{mean gradient mmHg}}$)

CAVEAT: Concomitant MR: calculate stroke volume by angiographic method

VALVULAR REGURGITATION

REGURGITANT VOLUME = Angiographic stroke volume (end-diastolic volume - end-systolic volume) - Net anterograde stroke volume (Fick or Thermodilution)

REGURGITANT FRACTION = Regurgitant volume / Angiographic stroke volume

SEMIQUANTITATIVE ANGIOGRAPHIC EVALUATION (ventriculography or aortography)		
GRADE	Regurgitant fraction	Opacification of the proximal chamber
1	< 20 %	<ul style="list-style-type: none"> • Slight opacification • Rapid elimination of contrast at each beat
2	21-40 %	<ul style="list-style-type: none"> • Moderate opacification • Density less than that of the proximal chamber • Rapid elimination of contrast with subsequent beats
3	41-60 %	<ul style="list-style-type: none"> • Intense opacification • Similar density to that of the proximal chamber in 4-5 beats
4	> 60 %	<ul style="list-style-type: none"> • Intense and rapid opacification • Density greater than that of the proximal chamber in ≤ 3 beats • \pm PV reflux in the presence of MR

INTRACARDIAC SHUNT

Level of L→R shunt	Increased SaO ₂ (step-up)	Example
Screening	PA SaO ₂ - SVC SaO ₂ ≥ 8%	Shunt at any level between the SVC and the PA
Atrial	RA SaO ₂ - mixed venous SaO ₂ ≥ 7%	ASD; Partial anomalous pulmonary venous connection; Ruptured aneurysm of the sinus of Valsalva; VSD + TR; Coronary fistula to RA
Ventricular	RV SaO ₂ - RA SaO ₂ ≥ 5%	VSD; Patent ductus arteriosus + PR; Primum ASD; Coronary fistula to RV
Pulmonary artery	PA SaO ₂ - RV SaO ₂ ≥ 5%	Patent ductus arteriosus; Aortopulmonary window; Palliative shunt (Pots; Waterston)

QP / QS: Pulmonary blood flow / Total systemic blood flow

$$QP / QS = Ao \text{ SaO}_2 - \text{mixed venous SaO}_2 / PV \text{ SaO}_2 - PA \text{ SaO}_2$$

$$\text{MIXED VENOUS SaO}_2 = 3/4 \times \text{SVC SaO}_2 + 1/4 \times \text{IVC SaO}_2$$

$$PV \text{ SaO}_2 \approx Ao \text{ saturation in the absence of R} \rightarrow \text{L shunt}$$

Qp / Qs < 1.5	Qp / Qs 1.5 - 2	Qp / Qs > 2
Small L→R shunt	Moderate L→R shunt	Large L→R shunt

OXIMETRIC RUN: SVC (2 x); IVC (2 x); RA (3 x); RV (3 x); main PA; RPA; LPA; LV; Ao; ± PV and ± LA

SCREENING OF R→L SHUNT: Ao SaO₂ < 95% despite FiO₂ = 100%

1.10/ NUCLEAR MEDICINE

SPECT MYOCARDIAL PERFUSION IMAGING

SPECT: Single-Photon Emission Computed Tomography

PRINCIPLE: Injection of a radioisotope (at rest then on exercise) → extraction by viable perfused myocytes → **emission of photons proportional to myocyte perfusion**

THREE STANDARD PERPENDICULAR PLANES: **A)** Short axis (apex to base); **B)** Vertical long axis (septum to lateral wall); **C)** Horizontal long axis (inferior wall to anterior wall)

ARTIFACTS / FALSE-POSITIVES: **A)** Movement during acquisition; **B)** Extraction of radioisotope by visceral organs; **C)** LBBB (use pharmacological stress); **D)** Septal HCM (relative perfusion deficit in lateral wall compared to hypertrophied septum); **E)** Dilated cardiomyopathy or HCM (zones of fibrosis; endothelial dysfunction); **F)** Attenuation

- **Attenuation by interposed structure:** **A)** Breasts → anterior / anterolateral attenuation; **B)** Diaphragm → inferobasal attenuation (improvement when patient upright)
- **Rule out attenuation:** **A)** Raw cine mode (look for interposed structure); **B)** Ventricular function (real perfusion deficit unlikely if normal wall motion on stress test)
- **Normal variants:** Membranous basal septum (less perfused); Apical thinning; Lateral wall appears to be better perfused than the septum (closer to the camera)

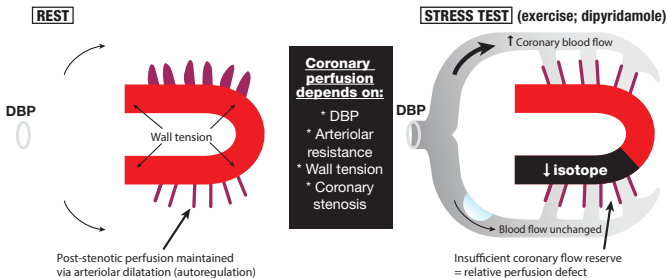
	201–Thallium	99m Technetium
Molecule	Cation; similar properties to K^+	<ul style="list-style-type: none"> Fat-soluble cationic compound Sestamibi and Tetrofosmin
Photon energy	80 keV	140 keV
Half-life	73 h	6 h
First-pass myocardial extraction	<ul style="list-style-type: none"> 85 % Perfusion-dependent Via Na-K-ATPase pump 	<ul style="list-style-type: none"> 60 % Perfusion-dependent Passive myocardial extraction (radioisotope trapped in mitochondria)
Myocardial redistribution	<ul style="list-style-type: none"> Imaging 3–4 h or 24 h post-injection Clearance of radioisotope is slower in ischemic myocardium ("differential washout") 	Minimal (2 injections are therefore necessary: stress test and at rest)
Protocol	<ol style="list-style-type: none"> Detection of ischemia: Injection on stress test with imaging #1; imaging #2 post-redistribution Viability study: Injection at rest with imaging #1; imaging #2 post redistribution (re-injection at this time to improve sensitivity) 	<ol style="list-style-type: none"> Same day: injection at rest (8–10 mCi) with imaging #1; injection on stress test with imaging #2 (22–30 mCi) 2 days: injection at rest (20–30 mCi) with imaging #1; injection on stress test (20–30 mCi) with imaging #2 Combined with Thallium: Injection of Thallium at rest with imaging #1; imaging #2 4h pre-Technetium (redistribution; viability study); injection of Technetium on stress test with imaging #3 (to detect ischemia)

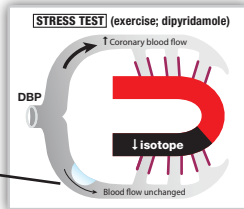
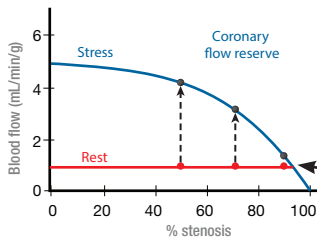
DIPYRIDAMOLE PHARMACOLOGICAL STRESS TEST: \nearrow intracellular adenosine \rightarrow stimulation of smooth muscle cell adenosine A2a receptors \rightarrow \nearrow cAMP \rightarrow coronary arteriolar vasodilatation \rightarrow \nearrow coronary blood flow

\triangleright **Dose:** 142 μ g/kg/min x 4 min (then inject isotope 3 min later)

\triangleright **Adverse effects:** \searrow SBP and \searrow DBP (8–10 mmHg); reflex tachycardia (\nearrow 10–20 bpm); minimal increase of double product (i.e. slightly \nearrow O_2 demand); flushing; retrosternal chest pain; asthma; blocks; real ischemia (in 10% of cases; coronary steal in ischemic collateral vessels)

\triangleright **Antidote:** aminophylline 1–2 mg/kg





HIGH RISK CRITERIA

- > **Negative test:** 1-year risk of death or myocardial infarction < 1% (exercise) or < 2% (dipyridamole)
- > **Resting LVEF:** < 35 %
- > **Extensive perfusion abnormality during stress:** ≥ 10% of the myocardium or involving ≥ 2 vascular territories
- > **Pulmonary uptake of ^{201}Tl (during stress):** marker of severe CAD (↗ wedge pressure and ↘ LVEF during stress)
- > **Transient LV dilatation (during stress):** ↗ ventricular chamber size; marker of severe CAD (↘ LVEF during stress and/or diffuse subendocardial ischemia)

VENTRICULAR FUNCTION: ECG-gated imaging → mean of hundreds of beats to obtain one cardiac cycle

RADIONUCLIDE VENTRICULOGRAPHY (RVG)

Evaluation of LVEF and RVEF

EQUILIBRIUM (MUGA): ECG gating; 99m Technetium-labeled RBC; mean of 1000 cycles; 3 standard views (anterior; LAO with optimal separation of RV and LV; lateral); evaluation of chamber dimension - regional wall motion - systolic function

- > **Systolic function:** estimated on biplane mode by counting photon emissions in the ventricle (diastole - systole / diastole)
 - **Systolic volume:** the count is proportional to ventricular volume (which can be estimated from a blood sample of a given volume and a given photon emission); measurement not influenced by ventricular geometry
- > **Diastolic function:** curve of ventricular volume as a function of time

FIRST-PASS: rapid bolus of Technetium 99m-DTPA → RA - RV → Lungs → LA - LV; can distinguish the activity of right and left (**better evaluation of the RV and shunt**); RAO view

POSITRON EMISSION TOMOGRAPHY


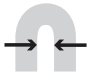






Quantitative evaluation of myocardial perfusion

ADVANTAGES VERSUS SPECT: better spatial resolution; better correction of attenuation; evaluates **absolute quantitative regional perfusion (mL/g/min)** (unlike SPECT which evaluates relative regional perfusion); better evaluation of balanced ischemia or microvascular disease

+

- > **Disadvantages:** requires a cyclotron; short half-life (pharmacological stress test only)
- > **^{82}Rb Rubidium:** cation with similar properties to those of the potassium and thallium; transport via Na-K-ATPase pump; half-life 75 s; perfusion-dependent myocardial extraction
- > **^{13}N ammonia:** passive diffusion or transport via Na-K-ATPase pump; half-life 10 min; perfusion-dependent myocardial extraction

VIABILITY STUDY: quantitative evaluation of myocardial metabolism (2-[¹⁸F]FDG); glucose extraction maintained in ischemic myocardium (anaerobic glycolysis); “mismatch” between myocardial perfusion and glucose metabolism in ischemic but viable (hibernating) myocardium +

MULTIMODAL EVALUATION OF VIABILITY			
DOBUTAMINE ECHOCARDIOGRAPHY	THALLIUM	CARDIAC PET	GADOLINIUM ENHANCED CARDIAC MRI
Hibernating myocardium: Biphasic response	Hibernating myocardium: Redistribution	Hibernating myocardium: Perfusion-metabolism discordance	Late gadolinium enhancement = scar (absence of viability)
<p>Resting</p>  <p>Baseline RWMA</p> <p>↓</p> <p>Dobutamine 5 µg/kg/min</p>  <p>Improvement</p> <p>↓</p> <p>Dobutamine 20 µg/kg/min</p>  <p>Deterioration</p>	<p>Resting</p>  <p>Relative perfusion deficit</p> <p>↓</p> <p>Redistribution</p>  <p>Differential washout</p>	<p>Resting</p>  <p>Relative perfusion deficit</p> <p>↕</p> <p>FDG metabolism</p>  <p>Glucose extraction maintained</p>	<p>Resting</p>  <p>Late gadolinium enhancement = scar</p>

1.11/ CARDIAC MAGNETIC RESONANCE IMAGING (CARDIAC MRI)

PHYSICAL PRINCIPLE: detects electromagnetic signals of nuclei of hydrogen atoms following application of a specific sequence of magnetic fields






PRECAUTIONS

CONTRAINDICATIONS: ferromagnetic material (stents and valve prosthese safe); www.mrisafety.com

➤ **Pacemaker and defibrillator (before new compatible generation):** contraindication to MRI; risk of arrhythmia; displacement of the device; inhibition; inappropriate shock; lead injury; battery depletion...

GADOLINIUM: risk of nephrogenic systemic fibrosis if $\text{CrCl} < 30 \text{ mL/min/1.73 m}^2$

TISSUE CHARACTERIZATION

T1	Fat content: ARVD; myocardial mass	
T2	Myocardial water content: acute myocarditis; acute myocardial infarction (high-risk zone); graft rejection	
T2*	T2* < 20 msec: (associated with LV dysfunction) compatible with iron overload cardiomyopathy (repeated transfusions; hemochromatosis)	
T1 Gadolinium-enhanced	Visualization of intravascular (blood) and extravascular water (myocardium) <ul style="list-style-type: none"> • First pass: myocardial perfusion • Early gadolinium enhancement (EGE): sign of inflammation (myocarditis; acute myocardial infarction) • Late gadolinium enhancement (LGE): 15 minutes post-redistribution; sign of fibrosis / myocardial necrosis 	
Ischemic heart disease	LGE: subendocardial or transmural scar	
Nonischemic cardiomyopathy	LGE: non-subendocardial scar	
HCM	LGE: scars in hypertrophied regions or in IV septum or close to the insertion of the RV	
Amyloidosis	<ul style="list-style-type: none"> • Rapid accumulation of contrast in the myocardium (rapid first-pass washout from blood) • LGE: circumferential subendocardial enhancement; transmural patchy enhancement • Late atrial enhancement 	
Sarcoidosis Myocarditis	<ul style="list-style-type: none"> • LGE: intramural or subepicardial or epicardial scar, sparing the endocardium • Sarcoidosis: anteroseptal and inferolateral walls often affected 	

INDICATIONS

CARDIOMYOPATHY / HEART FAILURE / MYOCARDITIS: dimensions; systolic and diastolic functions; segmental wall motion; measurement of deformation (strain); tissue characterization (sarcoidosis; myocarditis; amyloidosis; hemochromatosis); viability - scars (LGE); HCM; ARVD; LV noncompaction; Chagas...

CORONARY DISEASE: scar - viability (LGE); congenital anomaly of coronary arteries; coronary fistula; segmental wall motion (at rest and with dobutamine); first-pass gadolinium perfusion study (at rest and with dipyridamole); acute myocardial infarction (T2)

VALVULAR HEART DISEASE: stenosis (phase contrast is used to measure transvalvular velocities); regurgitation (volumetric method comparing RV and LV stroke volumes; phase contrast is used to measure antegrade and retrograde transvalvular velocities to calculate the regurgitant volume); perivalvular mass (fibroelastoma; vegetation; thrombus); complication of endocarditis; prosthetic valve dysfunction

CARDIAC MASSES: intracardiac thrombus (**non-vascularized**; absence of gadolinium enhancement); primary and secondary tumors (metastases)

PERICARDIAL DISEASE: constriction (paradoxical movement of the interventricular septum; ventricular interdependence; IVC distension); congenital absence of pericardium

CONGENITAL HEART DISEASE: anatomical assessment; structure - dimensions - function of chambers; conduits; shunts; Ao and PA

THORACIC AORTA: aneurysm; ulcer; dissection; CoA; aortitis; post-surgery; intramural thrombus

1.12/ CARDIAC CT

UNENHANCED CORONARY CALCIUM SCAN

This technique estimates the global coronary atherosclerotic burden; **very high sensitivity but low specificity for significant coronary stenosis**; independent predictor of coronary events (score of 0 associated with excellent prognosis)

INDICATIONS: asymptomatic patient with intermediate risk of cardiac events (10-20% at 10 years)

+

- **Agatston score:** score > 300 confers a 10-year risk of myocardial infarction or cardiovascular mortality of 28% (score of 100-399 increases the risk x 4 versus score < 100; score > 400 increases the risk x 5)

CARDIAC CT ANGIOGRAPHY (CCTA)

STRUCTURES EVALUATED: heart chambers; ventricular function (R and L); coronary arteries; bypass grafts; aortic and pulmonary arteries; pericardium; other adjacent structures; congenital heart disease; congenital coronary artery anomalies; endocarditis; ARVD; prosthetic valve; cardiac mass / thrombus; pulmonary veins

CORONARY CT ANGIOGRAPHY: good spatial resolution (vessels > 1.5 mm); **excellent sensitivity for significant coronary stenosis (very high negative predictive value for CAD); stenosis identified is not necessarily hemodynamically significant** and is not necessarily associated with ischemia (FFR-CT under development); decreased specificity in the presence of significant calcifications (Agatston score > 400) or obesity or HR > 65 bpm or AF or stent; independent predictor of coronary events (negative CCTA associated with excellent prognosis); can be used to evaluate patency of coronary bypass grafts; no difference on clinical outcome between CCTA vs. Functional testing in patients with suspected CAD (★ PROMISE)

+

- > **Indication: A)** Patient with no history of CAD presenting with retrosternal chest pain and intermediate pretest probability (especially when other noninvasive tests are inconclusive); **B)** Patient with low to moderate risk ACS (★ROMICAT-II); **C)** Rule out congenital anomaly of coronary arteries; **D)** Potential value for pre-op assessment before cardiac surgery when bypass graft is not planned (rule out significant CAD)

1.13/ CARDIOPULMONARY EXERCISE TESTING

Global evaluation of the oxygen transport system

INDICATIONS: A) Pre-transplantation assessment; **B)** Distinguish cardiac dyspnea from pulmonary dyspnea

PROTOCOL: Naughton; ↗ 1 MET every 2 min

FICK EQUATION

$$VO_2 \text{ MAX} = \text{HR} \times \text{Stroke volume} \times \left(\text{Maximum O}_2 \text{ content} - \text{Minimum O}_2 \text{ content} \right)$$

• 220 - age
 • Chronotropic incompetence

• PaO₂ - Pulmonary disease
 • Hemoglobin
 • SaO₂

• Contractility - LV dysfunction
 • Afterload
 • Preload
 • Valvular heart disease

• Skeletal muscle

PARAMETERS MEASURED: VO₂ (O₂ consumption); VCO₂ (CO₂ production); VE (minute ventilation); HR; BP; RR; SaO₂; PFTs; exercise ECG

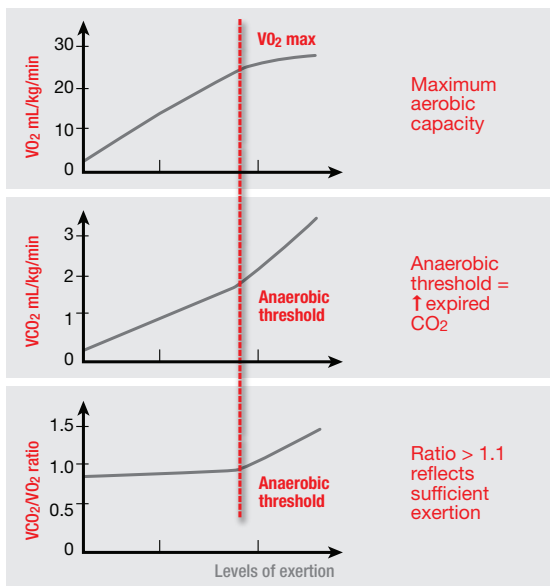
> **Ventilatory anaerobic threshold (VAT):** value of VO₂ when the slope of VE (or the slope of VCO₂) increases disproportionately to the slope of VO₂ (↗ CO₂ to be expired secondary to anaerobic glycolysis with formation of lactate); often at 50-60% of VO₂max (point at which dyspnea is experienced); activities of daily living situated below the VAT

> **Respiratory exchange ratio (VCO₂/VO₂):** ratio > 1.05 means that the patient has achieved adequate exertion +

> **VE/VCO₂ slope:** slope > 35 associated with poor prognosis; reflects hyperventilation secondary to V/Q abnormalities with ↗ dead space +

> **Borg scale:** quantification of the exertion perceived by the patient; > 18 / 20 = maximum exertion; > 15-16 / 20 = anaerobic threshold reached

	VO ₂ MAX	ANAEROBIC THRESHOLD	MAXIMUM CARDIAC INDEX
Heart failure with good prognosis	> 18 mL O ₂ /kg/min	> 14 mL O ₂ /kg/min	> 8 L/min/m ²
High-risk heart failure (consider transplantation)	< 10 mL O ₂ /kg/min (anaerobic threshold reached)	< 8 mL O ₂ /kg/min	< 4 L/min/m ²
Gray zone	VE/VCO ₂ slope > 35 associated with poor prognosis		



1.14/ EXPOSURE TO RADIATION DURING CARDIAC EXAMINATIONS

CXR (PA - lateral)	0.1 mSv
Diagnostic coronary angiography	7 mSv
PCI (or RF ablation)	15 mSv
Coronary CT angiography	5 mSv
Coronary calcium scan	3 mSv
MibiP	9.4 mSv
Thallium (stress - redistribution)	41 mSv
FDG PET	8 mSv
V/Q scintigraphy	2.2 mSv
CT pulmonary angiography	15 mSv
Radionuclide ventriculography (equilibrium)	7.8 mSv

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Coronary artery disease (CAD) & Myocardial infarction

02

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2.1/ STABLE ANGINA

O₂ DEMAND

- HR
- Wall stress (preload; afterload)
- Contractility



O₂ SUPPLY

- Coronary perfusion pressure (DBP – LVEDP)
- Patent coronary arteries
- Blood O₂ content

ANGINA: Clinical diagnosis



Constrictive retrosternal chest pain	On exertion (or emotions)	Relieved by rest (5–10 min) or nitrates
Typical chest pain = 3	Atypical chest pain = 2	Nonanginal chest pain = 1

CLINICAL HISTORY: Nature; Site; Radiation; Tempo; Duration; Modifiers; Associated symptoms (cardiovascular; respiratory; gastrointestinal)

SEVERITY OF ANGINA

CCS 1/4	Ordinary activity does not cause angina	≥ 7 METs • Angina occurs with strenuous or rapid or prolonged exertion only
CCS 2/4	Slight limitation of ordinary activity	5–7 METs • ≥ 2 flights of stairs • Walking ≥ 3 blocks on the level (or walking uphill) • Exertion after meals or in cold weather
CCS 3/4	Marked limitation of ordinary activity	2–5 METs • ≤ 1 flight of stairs • Walking one or two blocks on the level
CCS 4/4	Inability to carry out any physical activity without discomfort or angina at rest	< 2 METs • Any activity • Walking several steps

ANGINA EQUIVALENT: Dyspnea; Tiredness

CHARACTERISTICS NOT IN FAVOR OF CARDIAC CHEST PAIN: Pleuritic; Abdominal; Localized; Reproduced on palpation; Reproduced on movement; Duration < several seconds or > several hours

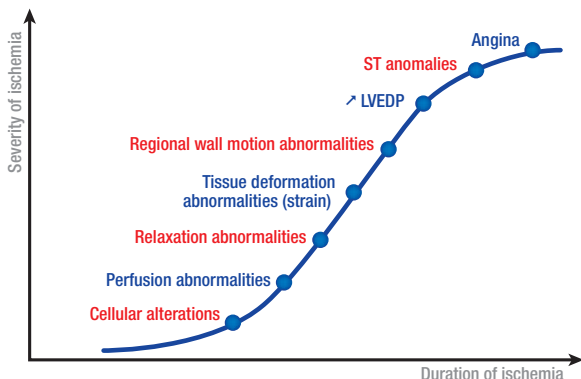
DDX: Aortic dissection; Aortic stenosis; HCM; Secondary ischemia (anemia; hyperthyroidism; arrhythmia); Cocaine; Pericarditis; Myocarditis; Takotsubo; Cardiac syndrome X (Microvascular); Pulmonary embolism; Pneumothorax; Pneumonia; PHT (RV ischemia); Pleurisy; Ruptured esophagus (Boerhaave); Pancreatitis; Cholecystitis; Cholelithiasis; Peptic ulcer (perforated); GERD; Esophageal spasm; Musculoskeletal; Costochondritis; Neck pain; Shoulder tendinitis; Shingles; Psychiatric

ASSESSMENT

TWO OBJECTIVES

- Confirm the diagnosis of CAD
- Establish the prognosis of the patient's CAD

ISCHEMIC CASCADE



PRETEST PROBABILITY OF SIGNIFICANT CAD on coronary angiography in a patient with retrosternal chest pain

AGE	NONANGINAL CHEST PAIN (≤ 1 CHARACTERISTIC)		ATYPICAL CHEST PAIN (2 CHARACTERISTICS)		TYPICAL CHEST PAIN (3 CHARACTERISTICS)	
	M	F	M	F	M	F
30-39	4 %	2 %	34 %	12 %	76 %	26 %
40-49	13 %	3 %	51 %	22 %	87 %	55 %
50-59	20 %	7 %	65 %	31 %	93 %	73 %
60-69	27 %	14 %	72 %	51 %	94 %	86 %

Diamond GA, Forrester JS. N Engl J Med 1979; 300:1350

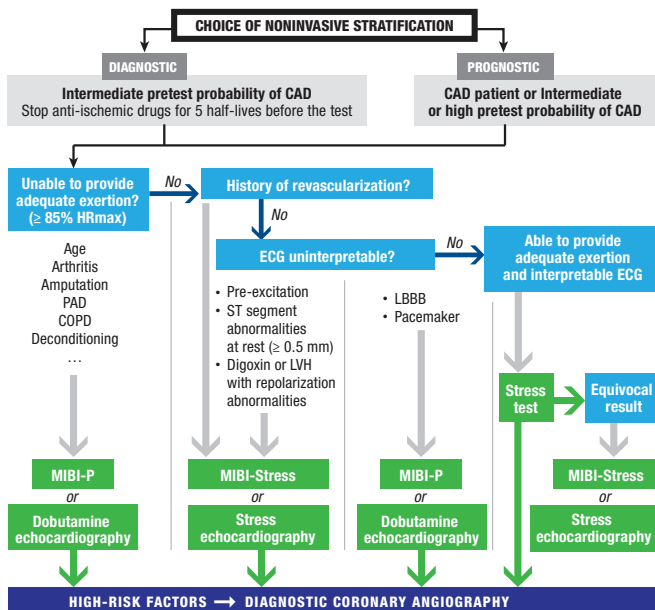
BAYES' THEOREM: the predictive value of a test depends on its sensitivity, specificity, and the pretest probability of the disease

- The diagnostic value of the test (when it is used to confirm the diagnosis of CAD) is maximal in patients with an **intermediate pretest probability of CAD (10-90%)**

02

Coronary artery disease (CAD) & myocardial infarction

CHOICE OF NONINVASIVE STRATIFICATION MODALITY



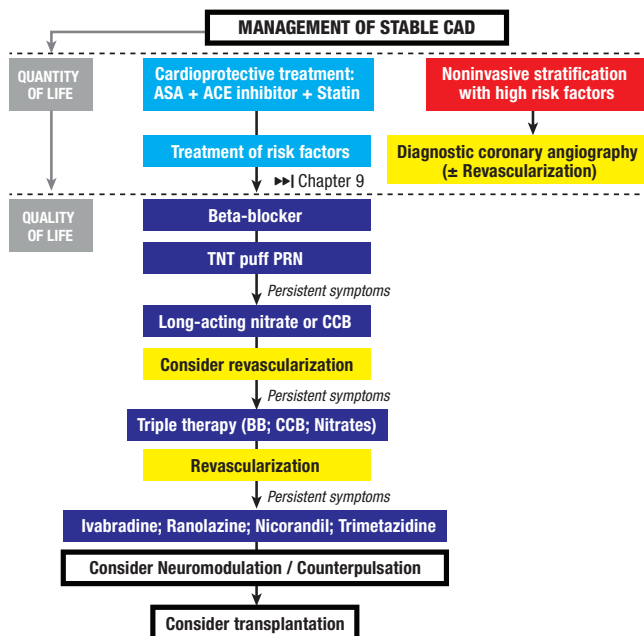
SENSITIVITY AND SPECIFICITY OF DIAGNOSTIC TESTS TO PREDICT SIGNIFICANT CORONARY ARTERY STENOSIS ON CORONARY ANGIOGRAPHY

	SENSITIVITY	SPECIFICITY
Stress test	68 %	77 %
MIBI–Stress	88 %	72 %
MIBI–Dipyridamole	90 %	75 %
Stress echocardiography	85 %	81 %
Dobutamine echocardiography	81 %	79 %
Coronary CT angiography	95 %	83 %

RISK ASSESSMENT DURING NONINVASIVE STRATIFICATION

<p>HIGH RISK (ANNUAL MORTALITY OR MYOCARDIAL INFARCTION > 3%)</p>	<ul style="list-style-type: none"> • LVEF: < 35% at rest (coronary cause) • LVEF: LV dysfunction during stress with LVEF at peak stress < 45% or \searrow LVEF \geq 10% • LV dilatation during stress • Stress test: Duke score \leq -11 • Stress test: ST depression \geq 2 mm (at low workload or persisting during recovery) or ST elevation or VT/VF on exercise • Echocardiography: regional wall motion abnormality during stress involving \geq 3 segments and/or \geq 2 vascular territories • Echocardiography: regional wall motion abnormality occurring at a low dose of Dobutamine (10 μg/kg/min) or at low HR (< 120 bpm) • MIBI: perfusion abnormality at rest involving \geq 10% of the myocardium (in the absence of a history of MI) • MIBI: perfusion abnormality on stress involving \geq 10% of the myocardium (or involving \geq 2 vascular territories) • Agaston score (non-contrast CT): > 400 • Coronary CT angiography: multiple vessel disease (stenosis \geq 70%) or LMCA involvement (stenosis \geq 50%)
<p>INTERMEDIATE RISK (ANNUAL MORTALITY OR MI: 1-3%)</p>	<ul style="list-style-type: none"> • LVEF: 35-49% at rest (coronary cause) • Stress test: Duke score: -10 to +4 • Stress test: ST depression \geq 1 mm + symptoms on exertion • Echocardiography: regional wall motion abnormality during stress on 1-2 segments (involving 1 vascular territory) • MIBI: perfusion abnormality at rest involving 5 to 9.9% of the myocardium (in the absence of a history of MI) • MIBI: perfusion abnormality on stress involving 5 to 9.9% of the myocardium (involving 1 vascular territory) • Agaston score (non-contrast CT): 100-399 • Coronary CT angiography: 1 vessel with stenosis \geq 70% (or \geq 2 vessels with 50-69% stenosis)
<p>LOW RISK (ANNUAL MORTALITY FROM MI < 1%)</p>	<ul style="list-style-type: none"> • Stress test: Duke score \geq +5 (or absence of ST abnormalities and symptoms with exercise achieving 85% of predicted HRmax) • Echocardiography: normal or limited regional wall motion abnormality at rest and unchanged during stress • MIBI: normal or small perfusion defect at rest or on stress involving < 5% of the myocardium • Agaston score (non-contrast CT): < 100 • Coronary CT angiography: absence of stenosis > 50%

MANAGEMENT



CARDIOPROTECTIVE TREATMENT

TREATMENT IMPROVING SURVIVAL: **A)** ACE inhibitors; **B)** ASA; **C)** Statin

ASA ★ Antithrombotic Trialists' Collaboration); Plavix if allergy (★ CAPRIE)

ACE INHIBITORS: ★ HOPE; ★ EUROPA; cardioprotective effect; particularly beneficial if LV dysfunction / DM / HTN / CRF

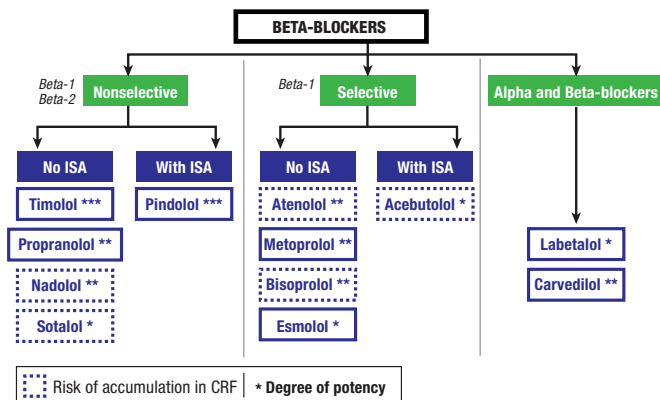
TREATMENT OF RISK FACTORS: ►► **Chapter 9**; HTN; Dyslipidemia (statins); DM; Smoking; Exercise program; Target healthy weight; Balanced diet

ANTI-ANGINAL TREATMENT

BB: first-line; antagonist of catecholamine adrenergic receptors; **negative inotropic and negative chronotropic agent** (↗ duration of diastole → ↗ coronary perfusion); anti-anginal; antihypertensive; antiarrhythmic

► **Intrinsic sympathetic activity (ISA):** partially beta-agonist at rest





NITRATES: converted into NO in the cell → ↑ intracellular cGMP → smooth muscle relaxation (by decreasing intracellular Ca^{2+}); **veinodilatation** (↓ preload); **coronary vasodilatation** (↑ perfusion); **systemic arterial vasodilatation** (↓ afterload)

CALCIUM CHANNEL BLOCKERS

- **Dihydropyridines:** Nifedipine (★ ACTION); Amlodipine (★ CAMELOT); **systemic arterial vasodilatation** (↓ afterload); **coronary vasodilatation** (↑ perfusion)
- **Nondihydropyridines:** Verapamil; Diltiazem; **negative inotropic and negative chronotropic agent**; **systemic and coronary arterial vasodilatation**

IVABRADINE (PROCORALAN): sinus node I_f channel inhibitor; ↓ HR (↑ duration of diastole → ↑ coronary perfusion); ★ INITIATIVE; ★ ASSOCIATE; ★ SIGNIFY: no effect on CV death or MI (but ↑ primary end point among patients with angina of CCS class ≥ 2/4)

RANOLAZINE (RANEXA): ↓ myocyte calcium overload by I_{Na} inhibition; anti-anginal (★ CARISA; ★ ERICA; ★ MERLIN-TIMI 36)

NICORANDIL: 3 mechanisms: **A)** Opening of potassium channels of ischemic cells (mimics ischemic preconditioning); **B)** Opening of potassium channels allowing **systemic and coronary arterial vasodilatation**; **C)** Similar properties to Nitrates

- ★ IONA: Stable CAD; ↓ primary outcome with Nicorandil (cardiovascular mortality - MI - hospitalization)

TRIMETAZIDINE (VASTAREL): fatty acid oxidation inhibitor; ★ TRIMPOL II

EXTERNAL COUNTERPULSATION: 35 one-hour treatments for 7 weeks; cuffs on lower limbs that inflate in early diastole and deflate in pre-systole; ↑ **collateral circulation and/or angiogenesis and/or improvement of endothelial function**

- **Contraindications:** active DVT; PAD; Aortic aneurysm; Aortic stenosis; Aortic regurgitation; Uncontrolled HTN; Decompensated heart failure

NEUROMODULATION: Spinal cord stimulation (T1-T2); ↓ **nociceptive transmission to CNS**

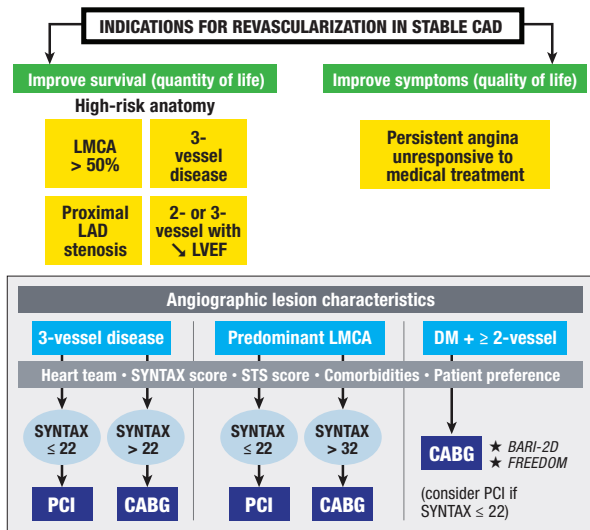
LASER MYOCARDIAL REVASCLARIZATION DURING CARDIAC SURGERY (THERAPEUTIC ANGIOGENESIS): create subendocardial channels by left intraventricular laser; consider during refractory angina in the presence of a nonrevascularizable ischemic territory; used exceptionally

ANTI-ANGINAL	DOSES	ADVERSE EFFECTS
BETA-BLOCKERS	<p>Target resting HR 50-60 bpm</p> <p>Maintenance dose</p> <ul style="list-style-type: none"> • Metoprolol: 50 - 100 mg bid • Bisoprolol: 2.5 - 10 mg qd • Carvedilol: 3.125 - 50 mg bid • Atenolol: 50 - 100 mg qd • Propranolol LA: 80 - 320 mg qd • Nadolol: 40 - 240 mg qd • Esmolol: Bolus IV 500 µg/kg; infusion 50 - 200 µg/kg/min 	Bradycardia - Blocks; Negative inotropic agent (heart failure); Bronchospasm; Depression / Tiredness; Nightmares; Erectile dysfunction; masked symptoms of hypoglycemia (prefer Bisoprolol or Metoprolol); rebound ischemia after sudden discontinuation; Possible exacerbation of PAD or Raynaud or Prinzmetal (unopposed alpha stimulation); ↗ TG and ↘ HDL (nonselective BBs)
NITRATES	<ul style="list-style-type: none"> • Sublingual: 0.4 mg/puff every 5 min x 3 • Patch: 0.2 - 0.8 mg/h; 8:00 a.m. to 8:00 p.m. • Isosorbide 5-mononitrate (Imdur): 30 to 240 mg qd • Isosorbide dinitrate: 10 - 40 mg tid • IV: 5 - 200 µg/min 	Headache; Flushing; Hypotension; Tolerance (prevention by 12-hour period without TNT each day); Methemoglobinemia; Interaction with PDE5 inhibitors; Avoid in the presence of aortic stenosis or HCM
DIHYDROPYRIDINE CCBS	<ul style="list-style-type: none"> • Nifedipine SR (long-acting): 30 - 60 - 90 mg qd • Amlodipine: 2.5 - 10 mg qd 	Headache; Faintness; Hypotension; Flushing; Leg edema
NONDIHYDRO-PYRIDINE CCBS	<p>Diltiazem</p> <ul style="list-style-type: none"> • PO: 30 - 90 mg tid-qid • CD: 120 - 360 mg qd • Bolus: 0.25 mg/kg IV • Infusion: 5 - 15 mg/h <p>Verapamil</p> <ul style="list-style-type: none"> • PO: 80 - 120 mg tid-qid • SR: 120 - 480 mg qd • Bolus: 0.075 - 0.15 mg/kg 	Block; Bradycardia; Heart failure (negative inotropic agent); Hypotension; Flushing; Headache; Leg edema; Drug interactions
IVABRADINE	<ul style="list-style-type: none"> • 5 to 7.5 mg bid 	Bradycardia; Phosphenes
NICORANDIL	<ul style="list-style-type: none"> • 10-20 mg bid 	Ulcers; Nausea; Hypotension; Headache; Weakness; Flushing
TRIMETAZIDINE	<ul style="list-style-type: none"> • 20 mg tid or 30 mg bid 	Nausea; Vomiting; Parkinsonism
RANOLAZINE	<ul style="list-style-type: none"> • 500 to 1000 mg bid 	Drug interactions; Nausea; Weakness; ↗ QT (but ↘ delayed after-depolarizations)

REVASCULARIZATION

2 OBJECTIVES

- Improve quantity of life (prognosis)
- Improve quality of life (symptoms)



FACTORS AFFECTING THE PATIENT'S PROGNOSIS

- Markers of high risk on noninvasive stratification
- Significant ischemia (> 10% of LV)
- LV dysfunction
- Anatomical extent of CAD / Number of vessels involved

BENEFITS OF CABG VERSUS MEDICAL TREATMENT ON SURVIVAL: **A) LMCA;**
B) 3 vessels; C) 2 vessels with proximal LAD (★ Yusuf; ★ VA Cooperative; ★ CASS; ★ ECSS)

PCI VERSUS MEDICAL TREATMENT: ★ **COURAGE** → Stable CAD (30% with proximal LAD)
 → PCI vs medical treatment; similar survival and infarction rates; ↘ **angina with PCI**

CABG VERSUS PCI: similar mortality and infarction rates (in patients eligible for both procedures); ↗ reintervention with PCI; ↗ Procedural stroke with CABG (★ EAST; ★ BARI; ★ ARTS; ★ SOS; ★ BEST)

★ **SYNTAX:** 3-vessel CAD or LMCA (eligible for both procedures) → CABG vs PCI; **similar mortality**; ↗ MI and ↗ reintervention with PCI

SYNTAX score ≤ 22	SYNTAX score 23–32	SYNTAX score ≥ 33
Similar primary outcome with CABG and PCI	↗ adverse events with PCI	↗ adverse events with PCI

CABG VERSUS PCI FOR LMCA: ★ SYNTAX subgroup (patients eligible for both procedures); ↗ reintervention with PCI; ↗ Procedural stroke with CABG

2.2/ BIOMARKERS

Released following myocyte necrosis (myocyte injury)

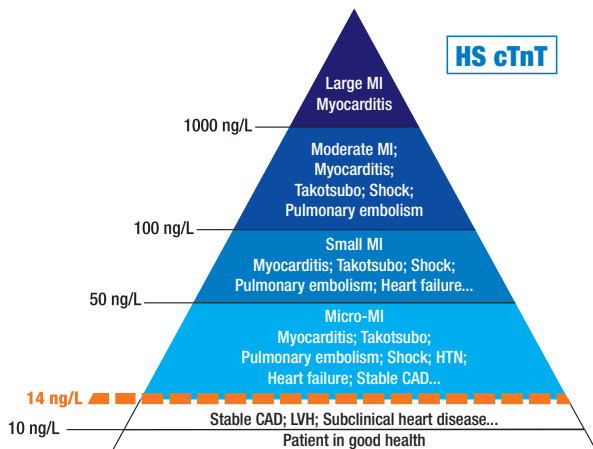
TROPONINS T AND I (CTNT AND CTNI): very sensitive and specific for myocyte necrosis but not very specific for myocardial infarction (ischemic myocyte necrosis)



MYOCYTE NECROSIS = LABORATORY DIAGNOSIS
MYOCARDIAL INFARCTION = CLINICAL DIAGNOSIS

DIFFERENTIAL DIAGNOSIS OF ELEVATED TROPONIN

- | | | |
|--------------------------------------|---------------------------------------|-----------------------------|
| • Infarction | • Aortic dissection | • Significant PHT |
| • Heart failure | • Coronary vasospasm | • Severe anemia |
| • Bradyarrhythmia or Tachyarrhythmia | • Endothelial dysfunction without CAD | • Respiratory failure |
| • Myocarditis | • PCI | • Intense physical exercise |
| • Pulmonary embolism | • Cardiac surgery | • Cardiotoxic chemotherapy |
| • Aortic valve disease | • Balloon valvuloplasty | • Cardiotoxins |
| • Myocardial contusion | • ECV / Defibrillation | • Subarachnoid hemorrhage |
| • Takotsubo | • Electrophysiological ablation | • Acute brain syndrome |
| • Infiltrative cardiomyopathy | • Graft rejection | • Rhabdomyolysis |
| • HCM | • Sepsis | • Body burn (> 30% BSA) |
| • Hypertensive crisis | • Renal failure | • Scorpion venom |

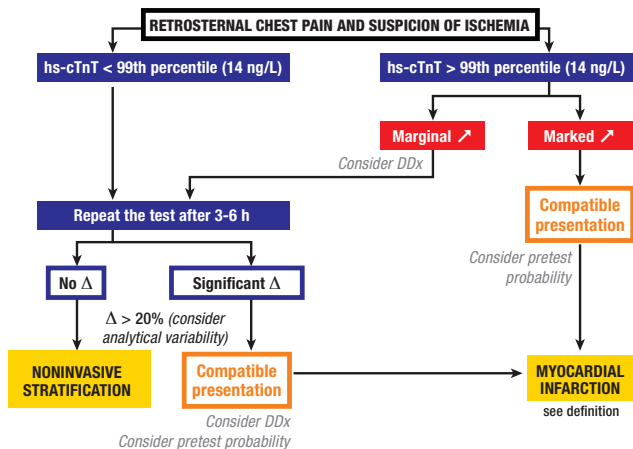


STANDARD TROPONIN: obtain a baseline value on arrival in the emergency room (0 h) and ≥ 1 value **> 6-9 h** after onset of chest pain



HIGH-SENSITIVITY TROPONIN: First troponin assay on arrival → sensitivity and specificity of 90% and NPV of 97%

- If hs-cTn negative on arrival (0 h) and 3-6 h after arrival with no significant difference between the two tests (< 20%) → NPV of 99%



REINFARCTION: assay Troponin at 0h - 3h - 6h; **diagnosis of reinfarction if** ↗ ≥ 20% (when cTn > 99th percentile pre-reinfarction but with stable or ↘ level)

	INITIAL ELEVATION	PEAK	RETURN TO NORMAL
CK-MB	3-12 h	24 h	48-72 h
Troponin I	3-12 h	24 h	5-10 d
Troponin T	3-12 h	12 h-48 h	5-14 d
Myoglobin	1-4 h	6-7 h	24 h

2.3/ MYOCARDIAL INFARCTION: DEFINITION

NECROSIS OF THE MYOCARDIUM IN THE PRESENCE OF MYOCARDIAL ISCHEMIA

DIAGNOSTIC CRITERIA

Detection of ↗ and/or ↘ of a cardiac biomarker (preferably cTn) with ≥ 1 value > 99th percentile (coefficient of variation of the test ≤ 10%) in the presence of myocardial ischemia
+
≥ 1 of the following elements

- **Symptoms** compatible with ischemia
- **Δ ECG changes** compatible with ischemia (Δ ST-T abnormalities) or *de novo* LBBB
- *De novo* pathological **Q waves**
- **Imaging:** loss of viable myocardium or *de novo* RWMA
- Intracoronary **thrombus** (on coronary angiography or at autopsy)

CLASSIFICATION

TYPE 1	Acute coronary syndrome: primary coronary event <ul style="list-style-type: none"> • Plaque rupture / erosion / ulceration; Coronary dissection
TYPE 2	Infarction secondary to O₂ supply and demand imbalance <ul style="list-style-type: none"> • Anemia; Hypoxemia; Arrhythmia; HTN; Hypotension; Cocaine; Coronary spasm; Endothelial dysfunction; Coronary embolism
TYPE 3	Cardiac arrest / Sudden death <ul style="list-style-type: none"> • Symptoms suggestive of ischemia + • Δ ECG changes compatible with ischemia or <i>de novo</i> LBBB + • No biomarker assays
TYPE 4a	Infarction secondary to PCI <ul style="list-style-type: none"> • Symptoms suggestive of ischemia or ischemic ECG changes or angiographic findings compatible with procedural complication or imaging compatible with loss of viable myocardium or <i>de novo</i> RWMA + • Positive biomarkers <ol style="list-style-type: none"> a) \nearrow cTn $\geq 5 \times$ upper limit of normal ($> 99^{\text{th}}$ percentile) when baseline cTn normal ($< 99^{\text{th}}$ percentile) or b) \nearrow cTn $> 20\%$ when baseline value elevated ($> 99^{\text{th}}$ percentile) but stable
TYPE 4b	Infarction secondary to stent thrombosis
TYPE 5	Infarction secondary to CABG <ul style="list-style-type: none"> • \nearrow cTn $\geq 10 \times$ upper limit of normal ($> 99^{\text{th}}$ percentile) when baseline cTn normal ($< 99^{\text{th}}$ percentile) + • <i>De novo</i> Q waves or <i>de novo</i> LBBB or new coronary (or CABG) occlusion on coronary angiography or imaging compatible with loss of viable myocardium or <i>de novo</i> RWMA

CAUSES OF INFARCTION IN THE ABSENCE OF ATHEROSCLEROSIS

O₂ SUPPLY/DEMAND IMBALANCE: AS; AR; CO poisoning; Hyperthyroidism; Prolonged hypotension; Hypertensive crisis; Sepsis - Fever; Anemia; Respiratory failure; AV fistula; HCM; Tachyarrhythmia; Cocaine; Endothelial dysfunction

CORONARY EMBOLISM: Endocarditis (infective or non-infective); MVP; Intracardiac thrombus; Prosthetic valve; Myxoma; Iatrogenic; Paradoxical embolism; Fibroelastoma; Valvular calcification

ARTERITIS: Syphilis; SLE; Takayasu (coronary ostium); PAN; Kawasaki; RA; Ankylosing spondylitis; Giant cell arteritis; Scleroderma

➤ **SLE:** Arteritis; endothelial dysfunction; thrombosis (antiphospholipid syndrome); accelerated atherosclerosis; coronary aneurysm

TRAUMA: Laceration; Iatrogenic; Radiotherapy; Contusion

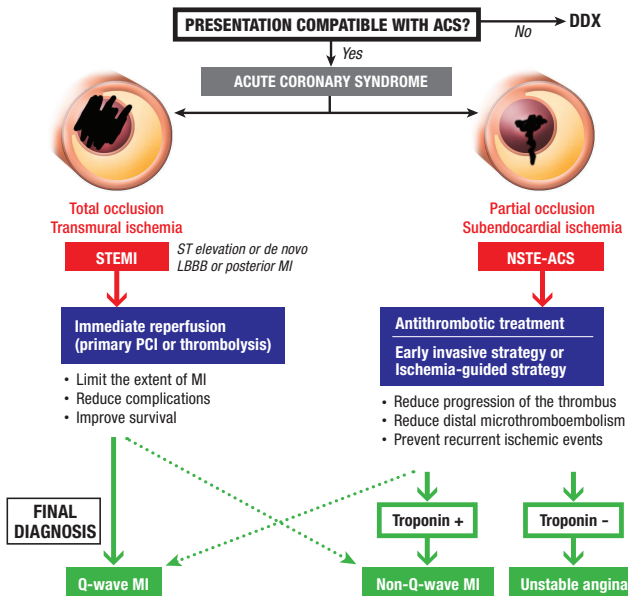
INFILTRATIVE / PROLIFERATIVE: Hurler's; Homocysteinuria; Fabry; Amyloidosis; Pseudoxanthoma elasticum

CONGENITAL: ALCAPA; Anomalous coronary origin; Coronary fistula; Coronary aneurysm

HEMATOLOGICAL (IN SITU THROMBOSIS): Hyperviscosity; Polycythemia; Thrombocytosis; Hypercoagulable state - Antiphospholipid syndrome; TTP; DIC

OTHER: Prinzmetal; Aortic dissection; Coronary dissection (pregnancy; Marfan; Ehlers-Danlos; Cocaine); Takotsubo; Thrombosis then spontaneous thrombolysis; Medications; Myocardial bridge

2.4/ UNSTABLE ANGINA & NSTEMI



IN-HOSPITAL MORTALITY of STEMI is 50% higher than that of NSTEMI

➤ **Similar one-year mortality for STEMI and NSTEMI** (high risk of recurrent events after NSTEMI)

PATHOPHYSIOLOGY: Rupture / Erosion of an unstable and friable atherosclerotic plaque with exposure of the subendothelial matrix then activation of primary and secondary hemostasis and thrombus formation

ASSESSMENT

SYMPTOMS OF ACS	UNSTABLE NATURE
<p>Retrosternal chest pain*</p> <ul style="list-style-type: none"> Nature: Constrictive - Tightness Radiation: Neck - Jaw - Upper limb Associated symptoms: Dyspnea; Nausea; Vomiting; Diaphoresis <p>* Atypical presentation / Anginal equivalent in elderly - DM - women</p>	<p>Any one of the following:</p> <ul style="list-style-type: none"> De novo angina < 2 months after presentation with CCS $\geq 3/4$ Crescendo angina: more frequent or longer or on less exertion (with CCS $\geq 3/4$) Angina at rest (often lasting > 20 min) < 1 week after presentation

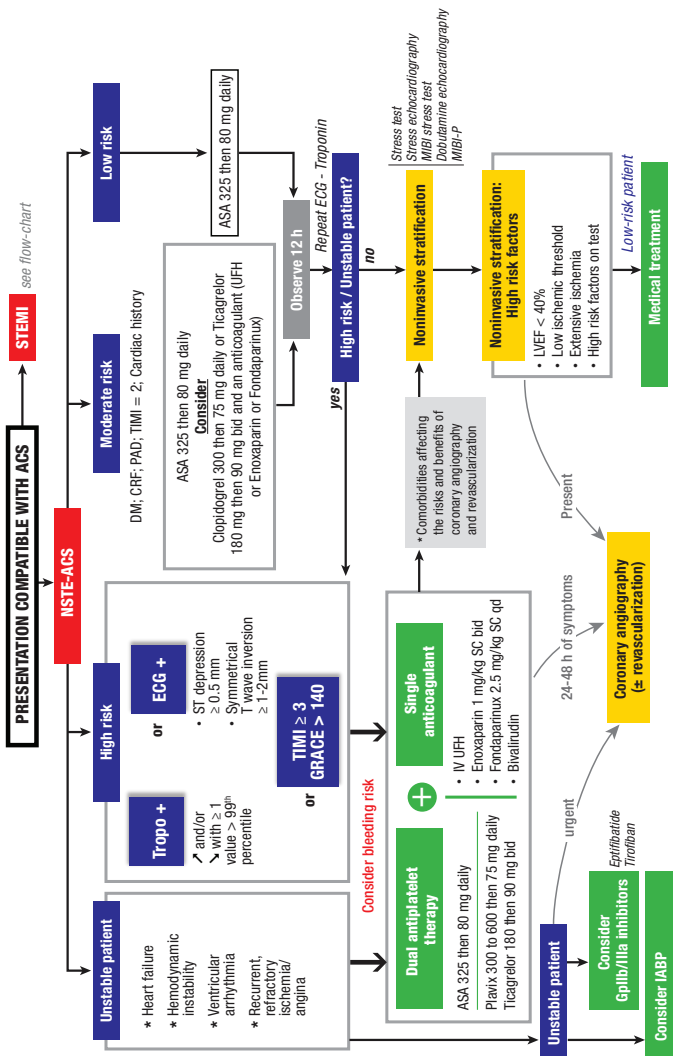
CLINICAL FEATURES: Diaphoresis; Cold skin; Sinus tachycardia; PVCs; \pm Hypotension; S3 or S4; Ischemic MR murmur; Crackles

ECG

ST depression	<ul style="list-style-type: none"> • Horizontal or descending • ≥ 0.5 mm (≥ 2 contiguous leads) 	+
T-wave inversion	<ul style="list-style-type: none"> • ≥ 1-2 mm (≥ 2 contiguous leads) ➢ Leads with R/S > 1 	

NSTE-ACS AND UNSTABLE ANGINA		
HIGH RISK (≥ 1 CRITERION)	INTERMEDIATE RISK (≥ 1 CRITERION)	LOW RISK
Unstable atherosclerotic plaque; Urgent evaluation		Outpatient stratification possible
<ul style="list-style-type: none"> • Accelerated angina < 48 h • Prolonged and persistent retrosternal chest pain at rest (> 20 min) • Ischemic pulmonary overload • <i>De novo</i> MR murmur • S3 or Crackles • Hypotension or Bradycardia or Tachycardia • Age > 75 years • Angina at rest with transient ST changes > 0.5 mm • <i>De novo</i> bundle branch block • Sustained VT • Significant elevation of troponins 	<ul style="list-style-type: none"> • History: myocardial infarction or PAD or cerebrovascular disease or history of CABG • Treatment with ASA • Prolonged retrosternal chest pain at rest (> 20 min) but resolved • Prolonged retrosternal chest pain (> 20 min), but resolved with rest or TNT • Nocturnal angina • CCS III or IV angina (<i>de novo</i> or progressive) < 2 weeks without prolonged retrosternal chest pain at rest (> 20 min) • Age > 70 years • T wave abnormalities • Pathological Q waves or ST depression at rest < 1 mm on multiple leads • Marginal elevation of troponins 	<ul style="list-style-type: none"> • More frequent or more severe or more persistent angina • Angina induced by a lower workload • <i>De novo</i> angina: between 2 weeks to 2 months before presentation • Normal ECG • Normal troponin

TIMI SCORE	GRACE SCORE
1) Age > 65 years 2) ≥ 3 risk factors for CAD 3) Known stenosis > 50% 4) ASA < 7 days 5) ≥ 2 episodes of retrosternal chest pain x 24 h 6) ST depression ≥ 0.5 mm 7) Biomarkers Death / MI / Urgent revascularization within 14 days 0-1 point.....4.7 % 2 points8.3 % 3 points13.2 % 4 points19.9 % 5 points26.2 % 6-7 points.....40.9 %	www.gracescore.org 1) Age 2) SBP 3) HR 4) Killip Class 5) Heart failure 6) Cardiac arrest at presentation 7) ST segment depression 8) Biomarkers 9) Creatinine In-hospital mortality GRACE ≤ 108 points.....< 1 % GRACE 109-140 points1-3 % GRACE > 140 points> 3 %



INITIAL MANAGEMENT

ARRIVAL IN THE EMERGENCY ROOM: ECG within 10 min; IV lines; Monitor; ASA 325 mg; Sublingual TNT (except when contraindicated); O₂ (for SaO₂ > 90%); ± Morphine 2.5 mg IV if persistent chest pain

CHOICE OF STRATEGY

EARLY INVASIVE STRATEGY	ISCHEMIA-GUIDED STRATEGY
<p>↘ Mortality; ↘ MI; ↘ Hospitalization (★ FRISC-II; ★ RITA-3; ★ TACTICS-TIMI 18)</p> <ul style="list-style-type: none"> • Unstable patient (urgent coronary angiography) <ul style="list-style-type: none"> ➢ Acute heart failure ➢ Hemodynamic instability ➢ Ventricular arrhythmia ➢ Recurrent and refractory angina/ischemia • Troponin + • Positive ECG (<i>De novo</i> ST depression) • Patient at high risk of recurrent events <ul style="list-style-type: none"> ➢ TIMI ≥ 3 ➢ GRACE > 140 • PCI < 6 months (rule out restenosis) • History of CABG (multiple anatomical possibilities) 	<p>According to non-invasive stress test (★ ICTUS)</p> <ul style="list-style-type: none"> • TIMI score 0-1 • GRACE < 109 • Risk of complications associated with coronary angiography and/or revascularization • Comorbidities; Frailty • Patient's preference

DUAL ANTIPLATELET THERAPY

ASA: Irreversible inhibitor of COX-1 (and TXA synthesis)

- ★ **Antithrombotic Trialists:** ↘ all-cause mortality; ↘ recurrent ischemic events
- **Dose:** 325 mg then 80 mg qd (★ CURRENT-OASIS 7)

CLOPIDOGREL: Second-generation thienopyridine; irreversible ADP P2Y₁₂ receptor antagonist

- ★ **CURE:** ↘ recurrent ischemic events (at 12 months); ↗ major bleeding
- ★ **CURRENT-OASIS 7:** High-dose clopidogrel (600 mg then 150 mg qd for 6 days then 75 mg qd) versus standard doses (300 mg then 75 mg qd) → potential benefit in **the subgroup of patients undergoing PCI** (but ↗ bleeding risk)
- **Disadvantage: A)** Slow onset of action (requires 2 metabolism and activation steps); **B)** Genetic polymorphisms of the cytochrome P450 enzyme responsible for metabolism (and activation) of clopidogrel (some patients metabolize and activate the medication less effectively); **C)** Inhibits 50-60% of platelets

TICAGRELOR: Reversible direct P2Y₁₂ receptor antagonist; rapid onset of action

- ★ **PLATO:** Ticagrelor versus clopidogrel (**47% of patients had received clopidogrel prior to randomization**); Revascularization or medical treatment → ↘ **all-cause mortality**; ↘ recurrent ischemic events; ↗ major bleeding not related to CABG
- **Adverse effects:** Dyspnea; ↗ ventricular pauses; ↗ creatinine (reversible)
- **Contraindication:** History of intracranial bleeding; active bleeding; severe liver disease; potent CYP3A4 inhibitor
- ★ **PEGASUS:** Ticagrelor (60 or 90 mg bid) versus Placebo in patients with a myocardial infarction 1-3 years earlier; ↘ **CV death - MI - Stroke** but ↗ **major bleeding**

PRASUGREL: no benefit in ★ ACCOAST (upfront therapy) and ★ TRILOGY ACS (ischemia-guided strategy)

GP1Ib/IIIA INHIBITORS : Block the formation of bridges between platelets (cross-links between GP1Ib/IIIA receptors and fibrinogen)

- > ★ **EARLY-ACS: no benefit** of eptifibatide initiated routinely > 12 h before coronary angiography versus eptifibatide initiated on demand during PCI
- > **Consider the use of GP1Ib/IIIA inhibitors** in patients treated with Ticagrelor (or Prasugrel): **during PCI for bailout situations / thrombotic complications**
 - **Eptifibatide: A)** Bolus: 180 µg/kg IV then 2nd bolus of 180 µg/kg within 10 min; **B)** Infusion: 2 µg/kg/min (initiated after 1st bolus); decrease the dose by 50% if GFR < 50 mL/min
 - **Tirofiban: A)** Bolus: 25 µg/kg IV; **B)** Infusion: 0.15 µg/kg/min; decrease the dose by 50% if GFR < 30 mL/min
 - **Abciximab: A)** Bolus: 0.25 mg/kg IV; **B)** Infusion: 0.125 µg/kg/min (max 10 µg/min)
- > **Adverse effects:** thrombocytopenia; bleeding

ANTICOAGULATION

Avoid crossover between antithrombins; stop anticoagulation after PCI (unless otherwise indicated)

UNFRACTIONATED HEPARIN

- > ★ **Eikelboom meta-analysis:** ↘ mortality (before the age of dual antiplatelet therapy and early revascularization)
- > **Doses:** 60 IU/kg bolus then 12 IU/kg/h; PTT every 6 h; target PTT 50-70 s (1.5 to 2 x control)
- **During coronary angiography:** additional UFH as needed (2000-5000 U); **A)** Absence of GP1Ib/IIIA inhibitors → target ACT 250-300 s (HemoTec) or 300-350 s (Hemochron); **B)** Presence of GP1Ib/IIIA inhibitors → target ACT 200-250 s
- > **Complications:** bleeding; HIT (consider Bivalirudin)

ENOXAPARIN (LMWH): Xa inhibitor and weak thrombin inhibitor (factor IIa inhibitor)

- > ★ **SYNERGY:** Enoxaparin vs Unfractionated heparin → ↗ **bleeding** during early invasive strategy with enoxaparin
- > **Doses:** 1 mg/kg SC bid (reduce to once daily if GFR < 30 mL/min)
- > **PCI:** Last dose > 8 h → 0.3 mg/kg IV bolus

FONDAPARINUX: indirect Xa inhibitor

- > ★ **OASIS-5:** Fondaparinux vs enoxaparin → ↘ bleeding; ↘ all-cause mortality; ↗ **catheter thrombosis during PCI** (as it does not act on already formed thrombin)
- > **Doses:** 2.5 mg SC once daily (avoid if GFR < 20 mL/min)
- > **PCI:** Add a bolus of unfractionated heparin (70-85 IU/kg; 50-60 IU/kg with concomitant GP1Ib/IIIA inhibitors)

BIVALIRUDIN: thrombin inhibitor (factor IIa inhibitor)

- > ★ **ACUITY:** Bivalirudin vs unfractionated heparin + GP1Ib/IIIA inhibitors → non-inferiority for primary outcome; ↘ major bleeding
- > ★ **MATRIX:** ACS with PCI anticipated; Bivalirudin vs unfractionated heparin → no benefit
- > **Dose: A)** Bolus: 0.1 mg/kg; **B)** Infusion: 0.25 mg/kg/h
- **During PCI: A)** Bolus: 0.5 mg/kg; **B)** Infusion: 1.75 mg/kg/h

RIVAROXABAN: oral Xa inhibitor

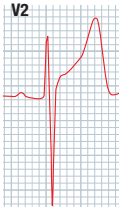
- > ★ **ATLAS ACS-TIMI 51:** Recent ACS on dual antiplatelet therapy; Rivaroxaban (2.5 or 5 mg bid; initiated an average of 4.5 days post-ACS) vs placebo; ↘ recurrent ischemic events; ↘ **all-cause mortality (2.5 mg bid)**; ↗ major bleeding
- > **Consider:** in combination with ASA and Clopidogrel (if Ticagrelor or Prasugrel are not available) in patients with high ischemic and low bleeding risks

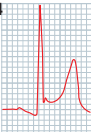
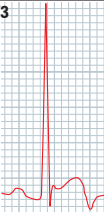
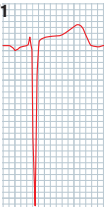


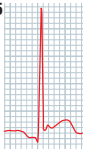
URGENT CORONARY ANGIOGRAPHY	EARLY INVASIVE STRATEGY (< 48 H)	ISCHEMIA-GUIDED STRATEGY
<ol style="list-style-type: none"> 1) ASA 325 mg 2) Ticagrelor 180 mg or Clopidogrel 600 mg 3) \pm GpIIb/IIIa inhibitors (during PCI for bailout situations) 4) Unfractionated heparin 	<ol style="list-style-type: none"> 1) ASA 325 mg 2) Ticagrelor 180 mg then 90 mg bid or Clopidogrel 300 mg then 75 mg qd (consider an additional 300 mg if PCI then 150 mg qd for 6 days then 75 mg) 3) Unfractionated heparin or Enoxaparin or Fondaparinux or Bivalirudin > Stop after PCI in the absence of complications 	<ol style="list-style-type: none"> 1) ASA 325 mg 2) Ticagrelor 180 mg then 90 mg bid or Clopidogrel 300 mg then 75 mg qd (consider an additional 300 mg if PCI then 150 mg qd for 6 days then 75 mg) 3) Unfractionated heparin (48 h or until PCI is performed) or Enoxaparin or Fondaparinux if bleeding risk (for the duration of hospitalization or until PCI is performed)
<ul style="list-style-type: none"> • Patient already on Clopidogrel: another loading dose of 300 to 600 mg if PCI planned • Patient on Warfarin: wait for INR < 2.0-2.5 before starting anticoagulant 		

2.5/ ST SEGMENT ELEVATION MYOCARDIAL INFARCTION (STEMI)

ECG CRITERIA

ST ELEVATION (FROM POINT J IN ≥ 2 CONTIGUOUS LEADS)	
V2 - V3	<ul style="list-style-type: none"> • Male ≥ 40 years: ≥ 2 mm • Male < 40 years: ≥ 2.5 mm • Female: ≥ 1.5 mm
All other leads	≥ 1 mm
V3R - V4R - V7 - V8 - V9	≥ 0.5 mm

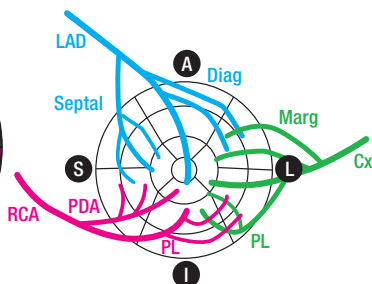
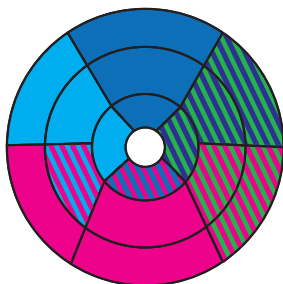
DDX OF ST ELEVATION		
Male ST pattern	<ul style="list-style-type: none"> • 90% of men < 35 years • Concave ST elevation > 1 mm in V1 to V3 (especially V2) 	

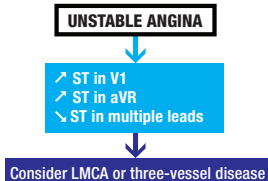
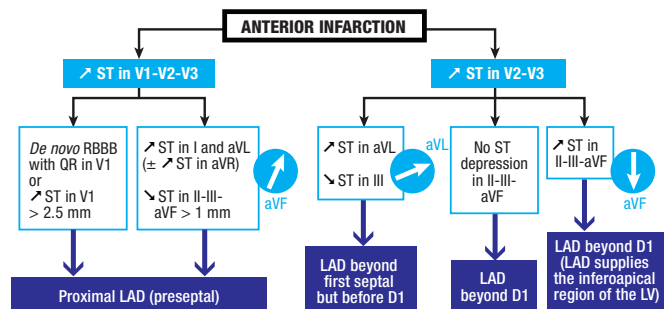
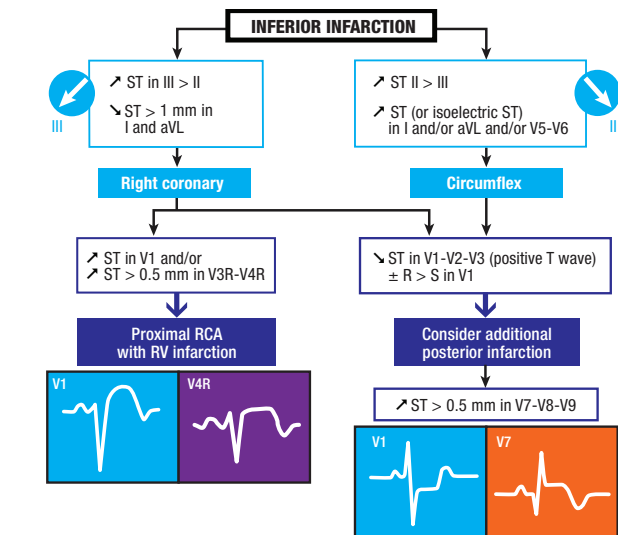
Early repolarization	<ul style="list-style-type: none"> • Large T waves (especially in V4) • ST elevation in V2-V3-V4 (concave) • Notch at point J • PR segment depression 	V4 
Juvenile T wave pattern and early repolarization	<ul style="list-style-type: none"> • T wave inversion (juvenile T wave pattern) combined with early repolarization • Short QT 	V3 
LVH	<ul style="list-style-type: none"> • Concave ST elevation in V1 to V3 • Positive voltage criteria 	V1 
Post-MI with aneurysm	<ul style="list-style-type: none"> • Persistent ST elevation (> 3 weeks post-MI) in the presence of Q waves 	V3 
LBBB (or paced rhythm)	<ul style="list-style-type: none"> • Concave ST elevation; the ST deviation is discordant with the QRS axis 	V1 
	<p>Sgarbossa criteria (infarction in the presence of LBBB)</p> <ol style="list-style-type: none"> 1) ST elevation ≥ 1 mm in leads with positive QRS (inappropriate concordance) <ul style="list-style-type: none"> - Criterion with the best predictive value 2) ST depression ≥ 1 mm V1-V2-V3 (inappropriate concordance) 3) ST elevation ≥ 5 mm in leads with negative QRS (extreme discordance) 	
Acute pericarditis	<ul style="list-style-type: none"> • Diffuse concave ST elevation (multiple anatomical territories) • PR segment depression • Reciprocal changes in aVR 	V5 

Brugada syndrome	<ul style="list-style-type: none"> • rSR' and ST elevation in V1 and V2 with descending slope and T wave inversion 	V2
Hyperkalemia	<ul style="list-style-type: none"> • Peaked and symmetrical T waves • ST elevation • Other signs: Wide QRS; decreased amplitude of P waves; blocks; asystole 	V4
Pulmonary embolism	<ul style="list-style-type: none"> • T wave inversion and ST elevation in right precordial and inferior leads • S1 Q3 T3 • RBBB • Sinus tachycardia 	V1

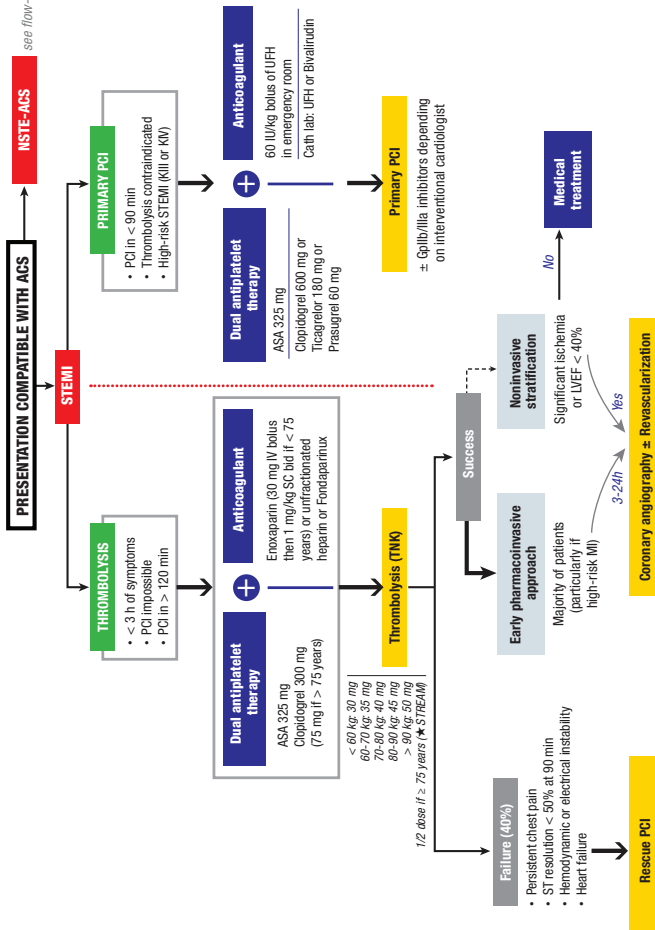
SITE OF INFARCTION ON ECG

I Lateral	aVR	V1 Antero-septal	V4 Anterior	V3R-V4R Right heart
II Inferior	aVL Lateral	V2 Antero-septal	V5 Antero-lateral	
III Inferior	aVF Inferior	V3 Anterior	V6 Antero-lateral	V7-V8-V9 Posterior





see flow-chart



INITIAL MANAGEMENT

EMERGENCY ROOM: ECG within 10 min; IV lines; Monitor; ASA 325 mg; Sublingual TNT (except when contraindicated); O₂ (for SaO₂ > 90%); ± Morphine 2.5 mg IV if persistent chest pain

KILLIP CLASSIFICATION

Killip I	No crackles; No S3
Killip II	Crackles (< 50% of lung fields) ± S3
Killip III	Crackles > 50% of lung fields
Killip IV	Cardiogenic shock

TIMI SCORE IN STEMI

CRITERIA	# POINTS	30-DAY MORTALITY
Age 65-74 years or ≥ 75 years	2 or 3 points	0 : 0.8 %
SBP < 100	3 points	1 : 1.6 %
HR > 100 bpm	2 points	2 : 2.2 %
Killip II-III-IV	2 points	3 : 4.4 %
History: DM or HTN or Angina	1 point	4 : 7.3 %
< 67 kg	1 point	5 : 12.4 %
Time to treatment > 4 h	1 point	6 : 16.1 %
Anterior STEMI or LBBB	1 point	7 : 23.4 %
		8 : 26.8 %
		> 8 : 35.9 %

IMMEDIATE REPERFUSION

THROMBOLYSIS	PRIMARY PCI
< 30 min after 1 st medical contact*	< 90 min after 1 st medical contact*
↘ Mortality (vs Placebo) (★ GISSI; ★ ISIS-2; ★ ASSET)	↘ Mortality (vs Thrombolysis) ↘ Recurrent infarction ↘ Risk of intracranial hemorrhage
Fibrinolysis less effective > 6 h after symptom onset <ul style="list-style-type: none"> • Early presentation: < 3 h of symptoms • Significantly delayed PCI (1st medical contact until PCI > 120 min) • PCI impossible (cath lab not available; vascular access impossible) 	<ul style="list-style-type: none"> • PCI available in < 90 min after 1st medical contact • > 3 h of symptoms • Contraindication to thrombolysis <ul style="list-style-type: none"> - Bleeding risk / Intracranial bleeding • High-risk STEMI • Doubtful diagnosis

* Including paramedics

THROMBOLYSIS

TENECTEPLASE (TNK): < 60 kg → 30 mg; 60-70 kg → 35 mg; 70-80 kg → 40 mg; 80-90 kg → 45 mg; ≥ 90 kg → 50 mg; if ≥ 75 years → **half dose** (★STREAM)

> ★ **ASSENT-2:** Tenecteplase vs tPA → ↘ major bleeding with TNK

TIME TO ADMINISTRATION: maximum benefit on mortality < 2-3 h of symptoms

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- > \ **Response of thrombus** to thrombolysis **after > 3 h of symptoms**
- > It is reasonable to perform thrombolysis up to 12-24 h after onset of symptoms in the presence of persistent ischemia (angina and \ ST on ECG) and significant infarction
 - ★ LATE - ★ EMERAS: \ **mortality between 6-12 h of symptoms**

ABSOLUTE CONTRAINDICATIONS	RELATIVE CONTRAINDICATIONS
<ul style="list-style-type: none"> • History of intracranial hemorrhage • Structural CNS vascular disease • Intracranial neoplasm • Stroke < 3 months • Suspicion of aortic dissection • Active bleeding (excluding menstruation) or bleeding diathesis • Significant facial / head trauma < 3 months • Intracranial or spinal cord surgery < 2 months • Severe refractory HTN 	<ul style="list-style-type: none"> • SBP > 180 mmHg and/or DBP > 110 mmHg • Stroke > 3 months or dementia or intracranial disease • CPR > 10 min or traumatic • Major surgery < 3 weeks • Internal bleeding < 2-4 weeks • Noncompressible vascular puncture • Pregnancy • Active peptic ulcer • Oral anticoagulant
<ul style="list-style-type: none"> • Risk of intracranial bleeding → Prefer PCI if ≥ 2 criteria present <p>1) > 65 years; 2) BP > 160-170/95; 3) M < 70 kg and F < 65 kg</p>	

PRIMARY PCI: ADJUVANT TREATMENT

ASA: 325 mg then 80 mg qd

CLOPIDOGREL: 600 mg then 75 mg qd

PRASUGREL: Third-generation thienopyridine; irreversible inhibition of the P2Y₁₂ receptor; one-step activation (versus 2 steps for clopidogrel); metabolism not affected by genetic polymorphisms of cytochrome P450 enzymes

- > ★ **TRITON-TIMI 38:** thienopyridine-naïve patients; known coronary anatomy (except if primary PCI) → \ ischemic events; \ stent thrombosis; \ major bleeding
- > **Avoid in patients:** > 75 years; < 60 kg; History of stroke - TIA

+

TICAGRELOL

- > ★ **PLATO:** Clopidogrel-naïve or non-naïve patients; \ all-cause mortality; \ recurrent ischemic events; \ stent thrombosis; \ major bleeding not related to CABG

GP1Ib/IIIA INHIBITORS: in the cath lab at **the interventional cardiologist's discretion** (significant thrombus; insufficient prior antiplatelet treatment; slow- or no-reflow; thrombotic complication)

- > **Abciximab:** **A)** Bolus: 0.25 mg/kg IV; **B)** Infusion: 0.125 µg/kg/min

UNFRACTIONATED HEPARIN: 60 IU/kg bolus (max 4000 IU) then IV infusion with target aPTT of 50-70 s (12 IU/kg/h; max 1000 IU/h)

- > **During coronary angiography:** **A)** Absence of GP1Ib/IIIA inhibitors → target ACT 250-300 s (HemoTec) or 300-350 s (Hemochron); **B)** Presence of GP1Ib/IIIA inhibitors → target ACT 200-250 s

BIVALIRUDIN: Thrombin inhibitor; used in cath lab

- > ★ **HORIZONS-AMI:** Bivalirudin vs UFH + GP1Ib/IIIA inhibitors; \ **all-cause mortality**; \ major bleeding
- > ★ **MATRIX:** ACS (55% STEMI) with PCI anticipated; Bivalirudin vs UFH → no benefit with Bivalirudin
- > **Dose:** **A)** Bolus: 0.75 mg/kg; **B)** Infusion: 1.75 mg/kg/h (decrease to 1 mg/kg/h if CrCl < 30 mL/min)

THROMBOLYSIS: ADJUVANT TREATMENT

ASA: 325 mg then 80 mg qd (long-term); ★ ISIS-2

CLOPIDOGREL: 300 mg (75 mg if > 75 years) then 75 mg qd (14 days to 1 year);
★ CLARITY-TIMI 28 and ★ COMMIT

ENOXAPARIN: ★ EXTRACT-TIMI 25 → **Enoxaparin superior to Unfractionated heparin** but
↗ major bleeding

- **Bolus:** 30 mg IV (< 75 years)
- **Maintenance:** 1 mg/kg SC bid (max 100 mg for first 2 doses) (if > 75 years: 0.75 mg/kg SC bid; max 75 mg for first 2 doses)
- **GFR < 30 mL/min:** 1 mg/kg SC once daily
- **Duration:** until discharge from hospital (or for one week or until revascularization)

FONDAPARINUX: 2.5 mg IV bolus then 2.5 mg SC once daily until discharge from hospital (or for one week or until revascularization); avoid if CrCl < 30 mL/min

- ★ **OASIS-6:** Fondaparinux vs Heparin; ↘ mortality; ↘ MI recurrence rate

UNFRACTIONATED HEPARIN: 60 IU/kg (max 4000 IU) then IV infusion for 48 h (or until revascularization) with target aPTT of 50-70 s (12 IU/kg/h; max 1000 IU/h)

EARLY PHARMACOVASIVE STRATEGY: immediate transfer post-thrombolysis for coronary angiography ± revascularization within 3 to 24 h

- ★ **TRANSFER-AMI** and ★ **CARESS-in-AMI:** ↘ recurrent ischemic events

RESCUE PCI: ★ REACT → ↘ recurrent MI; ↘ heart failure

- **Particularly beneficial if significant ischemic territory** (anterior MI; inferior infarction with RV involvement or with ST depression in V1-V3)

INTRACRANIAL HEMORRHAGE

- Stop all agents potentially responsible
- Brain imaging + Neurology / Neurosurgery consultation
- 10 units of cryoprecipitate (fibrinogen and fVIII) + 2 units of FFP (fV and fVIII) + Protamine (1 mg for every 100 units of heparin over the last 4 hours) + Platelet transfusion (6-8 units)
- ↘ Intracranial pressure (hyperventilation; Mannitol; head of bed to 30°; surgery)

2.6/ ACUTE CORONARY SYNDROME: ADJUVANT TREATMENTS

NITRATES: venodilator (↘ preload); **coronary vasodilator** (↗ perfusion); **arterial vasodilator** (↘ afterload)

- **Indications:** **A)** Ischemia / Recurrent angina; **B)** Significant HTN; **C)** Heart failure
- **Doses:** 0.4 mg sublingual every 5 min x 3 then IV infusion PRN (5-10 µg/min IV; increase by 10 µg/min every 5 min PRN up to a dose of 200 µg/min)
- **Contraindications:** SBP < 90 mmHg; HR < 50 bpm; HR > 100 bpm in the absence of heart failure; RV infarction; PDE-5 inhibitor (24 h for Sildenafil; 48 h for Tadalafil)

BETA-BLOCKERS: negative inotropic / negative chronotropic agent; ↘ O₂ demand

- ★ **MIAMI** - ★ **ISIS-1** - ★ **COMMIT** → ↘ mortality; ↘ recurrent ischemic events; ↘ VF
- **Start orally within 24 h of presentation**
- **Contraindications:** Signs of heart failure; Low output state; Risk of cardiogenic shock (> 70 years; SBP < 120 mmHg; Sinus tachycardia > 110 bpm; HR < 60 bpm; Late presentation); PR > 0.24 s; 2nd or 3rd degree AV block; Active asthma
- **Avoid BB with ISA**
- **Short-acting BB:** IV Esmolol
- **Verapamil or Diltiazem** as an alternative in the absence of contraindications and LV dysfunction

AGENT	INDICATION	DURATION	CAUTION
ASA	<ul style="list-style-type: none"> All patients with ACS (★ Antithrombotic Trialists' Collaboration) 	Long term	ASA allergy Peptic ulcer
Clopidogrel (75 mg qd)	<ul style="list-style-type: none"> Post-ACS (without Ticagrelor or Prasugrel) (★ CURE) 	<ul style="list-style-type: none"> 1 year if DES Up to 1 year if BMS or medical treatment BMS: minimum 2-4 weeks 	Clopidogrel allergy
Ticagrelor (90 mg bid)	<ul style="list-style-type: none"> Post-ACS (without Clopidogrel or Prasugrel) (★ PLATO) Consider > 1 year post MI in high-risk patients (★ PEGASUS) 	<ul style="list-style-type: none"> 1 year if DES Up to 1 year if BMS or medical treatment 	Dyspnea Ventricular pauses
Prasugrel (10 mg qd)	<ul style="list-style-type: none"> Post-ACS (without Clopidogrel or Ticagrelor) (★ TRITON-TIMI 38) 	<ul style="list-style-type: none"> 1 year if DES Up to 1 year if BMS 	Avoid if weight < 60 kg or > 75 years or history of stroke - TIA
ACE inhibitor	<ul style="list-style-type: none"> All patients with CAD (± HTN or DM or CRF) (★ HOPE; ★ EUROPA) Post-ACS with LVEF < 40% or heart failure (★ TRACE; ★ SAVE; ★ AIRE) 	Start within 24 h of presentation Long term	ARF; Hyperkalemia; Cough; Angioedema Contraindicated if SBP < 100 mmHg
ARB (Valsartan or Candesartan)	<ul style="list-style-type: none"> Intolerance of ACE inhibitors with LVEF < 40% or heart failure (★ VALIANT; ★ CHARM-Alternative) 	Long term	ARF; Hyperkalemia; Hypotension
Beta-blockers	<ul style="list-style-type: none"> All patients post-myocardial infarction (★ Freemantle meta-analysis) Post-ACS with LVEF < 40% (★ CAPRICORN) Residual coronary stenosis (anti-anginal) 	<ul style="list-style-type: none"> Long term if LV dysfunction or as antianginal Otherwise: ≥ 3 years Target HR 50-60 bpm; use BB without ISA 	Active heart failure AV block Asthma
Statins	<ul style="list-style-type: none"> All patients with ACS (★ PROVE IT-TIMI 22) 	<ul style="list-style-type: none"> Long term High-dose statin 	Myopathy Myositis Transaminase
Eplerenone (25 mg then 50 mg qd)	<ul style="list-style-type: none"> ACS with LVEF < 40% (with heart failure or DM) (★ EPHEsus) 	Long term	Hyperkalemia > 5 mmol/L GFR < 30 mL/min
TNT (Nitropuff)	<ul style="list-style-type: none"> All patients with coronary disease 	Long term	Avoid if hypotension or PDE-5 inhibitor
Warfarin	<ul style="list-style-type: none"> LV thrombus Significant LV dysfunction with extensive regional wall motion abnormalities or LV aneurysm (class IIb recommendation) 	3 months then reevaluate Long term if mobile / pedunculated thrombus	Target INR 2-2.5 in the presence of dual antiplatelet therapy Add PPI

GLYCEMIC CONTROL: target blood glucose **< 10 mmol/L (180 mg/dL)** (★DIGAMI); avoid hypoglycemia (★NICE-SUGAR) +

PPI (PREFER PANTOPRAZOLE): patient on dual antiplatelet therapy with ≥ 1 risk factor:

A) History of upper GI bleeding / ulcer; **B)** > 60 years; **C)** Anticoagulant or Corticosteroids or NSAID; **D)** *H. pylori* - positive

ANEMIA: target hemoglobin **> 70-80 g/L** +

AVOID NSAID

> **If unavoidable** (despite Acetaminophen; ASA; Narcotics) → **prefer nonselective NSAID** (Naproxen; Ibuprofen) +

AVOID HORMONE THERAPY

STRESS TEST BEFORE DISCHARGE FROM HOSPITAL

- > No angina / Heart failure / Arrhythmia for 48-72 h
- > **Submaximal stress test (3-5 days):** stop if HR ≥ 120 bpm or $\geq 70\%$ of predicted HRmax or ≥ 5 METs or Angina or Dyspnea or \searrow ST 2 mm or Hypotension or ≥ 3 consecutive PVCs
- > **Stress test limited by symptoms (3 weeks):** not guided by HR or METs

MANAGEMENT ON DISCHARGE FROM HOSPITAL

MANAGEMENT OF RISK FACTORS: ▶▶| Chapter 9

ADMISSION TO CARDIAC REHABILITATION CENTER

SMOKING CESSATION

CONTROL OF LIPIDS

- > **Lipid profile** on day 1 of ACS (\searrow TC and \searrow HDL within 24-48 h of ACS)
- > **Target:** High-dose statin; **target \searrow > 50% LDL** +

BP CONTROL: **< 140/90 mmHg** (< 140/85 mmHg in the presence of DM) +

DM CONTROL: **HbA1c < 7 %** +

WEIGHT: BMI: 18.5-24.9 kg/m²; waist < 102 cm (M) and < 88 cm (F) +

BALANCED DIET

PHYSICAL ACTIVITY: **30 minutes of moderate exercise (rapid walking) 5 times a week** +

- > Pre-training stress test if necessary depending on risk factors

INFLUENZA VACCINE annually

TREAT DEPRESSION post-IM

SICK LEAVE: determined case by case; 2 weeks to 10 weeks

SEXUAL ACTIVITY: resume after 7-10 days (equivalent to one flight of stairs)

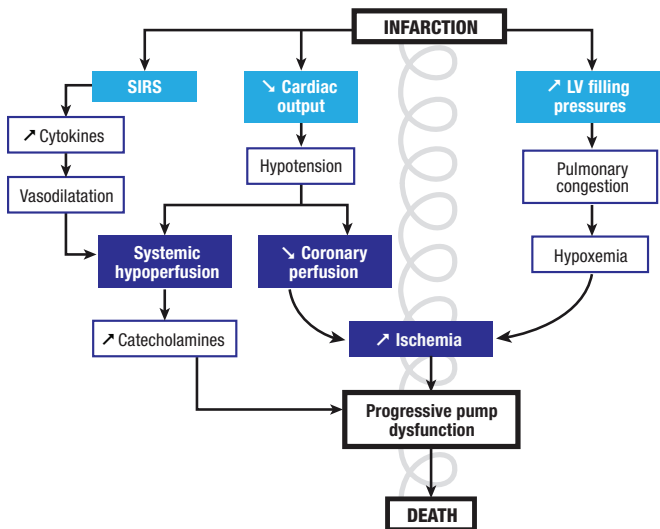
PLANE TRAVEL: ▶▶| Chapter 9

2.7/ COMPLICATIONS OF MYOCARDIAL INFARCTION

CARDIOGENIC SHOCK

02

Coronary artery disease (CAD) & myocardial infarction



↓ Cardiac output with inadequate tissue perfusion (despite sufficient filling pressures)

HEMODYNAMIC PARAMETERS

- > Hypotension (SBP < 90 mmHg)
- > Systemic hypoperfusion (cold extremities; altered level of consciousness; ↓ urinary output; $\text{SVO}_2 < 70\%$)
- > ↓ Cardiac Index (< 2.2 L/min/m²)
- > ↑ Filling pressures (Wedge pressure > 18 mmHg)

ETIOLOGIES: Extensive infarction; Mechanical complication; RV infarction

- > **DDx:** Hemorrhage; Pulmonary embolism; Tamponade; Sepsis; Myocarditis; Takotsubo; HCM; Endocarditis; Aortic dissection

MANAGEMENT

- > ★ **SHOCK:** ↓ mortality with early revascularization (< 75 years)

+

CXR POSITION: tip of the catheter **at the level of the carina** (> 4 cm below the aortic knob) **+**

CONTRAINDICATIONS: Moderate to severe AR; Aortic dissection; Significant abdominal aortic aneurysm; severe PAD; Uncontrolled sepsis

COMPLICATIONS: Aortic lesion / perforation; Bleeding at site of introduction; Ischemia distal to introducer (target the common femoral artery during introduction); Thrombocytopenia; Hemolysis; Atheroembolism; Renal ischemia; Cerebral ischemia in the case of proximal migration of the balloon; Infection

RIGHT VENTRICULAR INFARCTION

RV very resistant to ischemia (thin myocardium)

➤ **Excellent recovery of RV function post-MI**

CLINICAL FEATURES: Shock; ⬆ CVP (⬆ Y descent; mimics constrictive pericarditis); Kussmaul sign; Pulsus paradoxus; Clear lungs

HEMODYNAMIC PARAMETERS: Hypotension; ⬆ RA pressure / ⬆ RVEDP; ⬇ RV systolic pressure; ⬇ Wedge pressure; ⬇ Cardiac index

ECG: **ST elevation > 0.5-1 mm V3R and/or V4R** (in the context of infarction of the inferior wall of the LV); ± ST elevation in V1-V2 **+**

DDX: Pulmonary embolism (**absence of RWMA in inferior wall of LV**) **+**

COMPLICATIONS: R → L shunt (via PFO); Shock; Pulmonary embolism; Arrhythmia; AV block; Death

MANAGEMENT: **1)** Avoid TNT; **2)** Reperfusion; **3)** Bolus of normal saline to maintain adequate RV preload (attention to interdependence with LV; **avoid RVEDP > 15 mmHg**); **4)** Target Wedge pressure 15-18 mmHg; **5)** Inotropes (Dobutamine); **6)** Decrease RV afterload (avoid hypoxia; minimize PEEP; NO); **7)** Maintain AV synchrony (to ensure good filling of the ischemic RV and to increase RV output); **8)** IABP; RVAD; Impella; Creation of an ASD when necessary **+**

LEFT VENTRICULAR FREE WALL RUPTURE

One to 14 days post-transmural infarction

➤ **Secondary to extension of the infarction:** thinning and dilatation of the necrotic zone
➤ Often anterior or lateral LV wall

PRESENTATION: Pleuritic pain; Hypotension; Shock; Sudden death (pulseless electrical activity)

CLINICAL FEATURES: JVD; Pulsus paradoxus; Shock

TTE: signs of tamponade; look for the site of rupture

LEFT VENTRICULAR PSEUDOANEURYSM

Ventricular rupture contained by the pericardium and by thrombus / organized hematoma

Narrow neck (<< diameter of the pseudoaneurysm)

High risk of rupture and hemopericardium

LEFT VENTRICULAR ANEURYSM

Thinning of myocardium (but no rupture, in contrast with pseudoaneurysm)

Dyskinesia with paradoxical systolic expansion (alters the geometry and efficacy of contraction; ⬆ wall stress)

Large neck ($\geq 0.5 \times$ diameter of the aneurysm)

Low risk of rupture

ECG: persistent ST elevation

COMPLICATIONS: Embolism; Arrhythmia; Heart failure; Angina

INTRAVENTRICULAR THROMBUS

➤ **RISK OF EMBOLIZATION:** Mobile; Protrusion into the ventricle; Visualized on several sections; Contiguous zones of akinesia and hyperkinesia

MANAGEMENT: Anticoagulant therapy for 3-6 months then re-evaluate

VENTRICULAR SEPTAL RUPTURE

SITE

- **Anterior infarction** → apical interventricular septum
- **Inferior infarction** → inferobasal interventricular septum (less favorable prognosis)

PRESENTATION: Hypotension - Shock; Acute pulmonary edema; R and L heart failure; Blocks

CLINICAL FEATURES: Shock; **Prominent holosystolic murmur \pm thrill; S3;** Pulmonary edema; Signs of right heart failure

TTE: L→R shunt; RV insufficiency

CARDIAC CATHETERIZATION: **O₂ step-up between RA and RV;** Prominent V wave **+**

TREATMENT: Nitroprusside; IABP; Inotropes; Surgery vs percutaneous closure

PAPILLARY MUSCLE RUPTURE

Posteromedial papillary muscle (inferior infarction; supplied by PDA) >> anterolateral papillary muscle (double blood supply by LAD and circumflex) **+**

PRESENTATION: Hypotension; Shock; Acute pulmonary edema; **Systolic murmur, often minor** (early systolic equalization of transvalvular pressures) **+**

TTE (\pm TEE): Rupture of a papillary muscle or chorda tendineae; Leaflet eversion; Severe MR on Doppler; Hyperdynamic LV; PHT

CARDIAC CATHETERIZATION: **Prominent V wave;** ➤ **PAP** (\pm contaminated by V wave) **+**

TREATMENT: Nitroprusside; IABP; Inotropes; Mechanical ventilation; Urgent surgery

PERICARDITIS

EARLY: pericardial extension of transmural MI

- **Presentation:** Pleuritic pain radiating to the trapezius; **Pericardial friction rub;** **Localized ECG changes** **+**
- **Management:** Caution with anticoagulants (risk of hemorrhagic pericarditis; monitor by TTE); ASA 650 mg PO every 4-6 h; Colchicine

LATE (> 7 DAYS): Dressler's syndrome; Immune phenomenon

ARRHYTHMIAS AND BLOCKS

PVC: BB; Correct electrolyte disorders; No benefit of AAD (★ CAST; ★ SWORD)

MONOMORPHIC VT: Correct electrolyte disorders; BB; AAD; ECV; ICD if > 48 h (probable permanent arrhythmogenic substrate)

POLYMORPHIC VT: Rule out ischemia; Rule out ↗ QT; BB; Correct electrolyte disorders

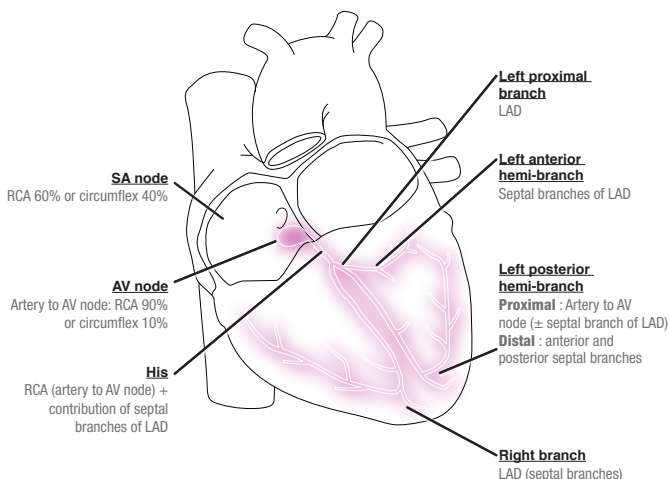
VF: Rule out ischemia; BB; AAD (Lidocaine; Amiodarone); ICD if > 48 h

AIVR: Ventricular rhythm 60-100 bpm; **Specific marker of reperfusion; Observation;** ↗ Sinus rhythm PRN (Atropine; Atrial pacing)

SINUS BRADYCARDIA: often associated with inferior STEMI (**Bezold-Jarish reflex**); Atropine; Atrial pacing

AV BLOCK AND INTRAVENTRICULAR BLOCKS

INFERIOR INFARCTION	ANTEROSEPTAL INFARCTION
RCA 90%; Circumflex 10%	Proximal LAD (± septal branches)
<ul style="list-style-type: none"> Mechanism: ↗ Vagal tone (< 6h; Bezold-Jarish) and/or AV node ischemia 	<ul style="list-style-type: none"> Mechanism: Extensive necrosis of the septum and conduction tissue (His-Purkinje system)
Bradyarrhythmias <ul style="list-style-type: none"> Sinus bradycardia Intranodal AV block <ul style="list-style-type: none"> 1st degree AV block or 2nd degree Mobitz I AV block or sometimes 3rd degree intranodal AV block 	Bradyarrhythmias <ul style="list-style-type: none"> Infranodal AV block <ul style="list-style-type: none"> 2nd degree Mobitz II AV block or 3rd degree infranodal AV block ↗ PR secondary to slowing of His-Purkinje conduction
<ul style="list-style-type: none"> Progressive onset of AV block 	<ul style="list-style-type: none"> Sudden onset of AV block (< 24 h); often preceded by RBBB ± LAHB
<ul style="list-style-type: none"> Junctional escape rhythm (His); narrow QRS; 40-60 bpm 	<ul style="list-style-type: none"> Escape rhythm distal to His bundle Wide QRS; unstable; risk of asystole
<ul style="list-style-type: none"> Often benign and transient (5-7 days) 	<ul style="list-style-type: none"> Often associated with extensive infarction
<ul style="list-style-type: none"> Atropine within the first 24 h (vagal hypertonia) Permanent pacemaker rarely indicated (reversible conduction disorder) 	Temporary pacemaker <ul style="list-style-type: none"> 2nd degree Mobitz II or 3rd degree AV block Alternating RBBB with LBBB Acute bifascicular block or <i>de novo</i> LBBB RBBB with ↗ PR Permanent pacemaker <ul style="list-style-type: none"> 2nd degree intra- or infranodal AV block with alternating branch block 3rd degree intra- or infranodal AV block Persistent 2nd or 3rd degree AV block with symptoms High-grade transient infranodal 2nd degree or 3rd degree AV block with associated branch block (except for isolated left anterior hemiblock)



2.8/ REVASCULARIZATION - PCI

SIGNIFICANT STENOSIS

ANGIOGRAPHIC	HEMODYNAMIC	IVUS (INTRAVASCULAR ULTRASOUND)
$\geq 70\%$ (LMCA: $\geq 50\%$)	$FFR \leq 0.80$	• LMCA: Area $< 6 \text{ mm}^2$ (6 to $7.5 \text{ mm}^2 \rightarrow$ determine FFR) • Other vessels: Area $< 4 \text{ mm}^2$

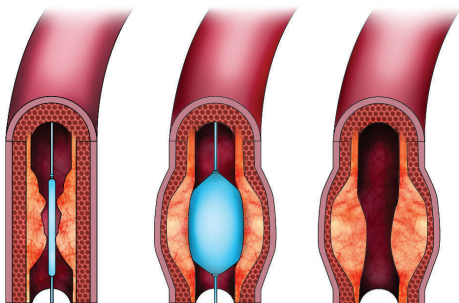
TECHNIQUES

BALLOON ANGIOPLASTY (PTCA): stretches / tears / redistributes the atherosclerotic plaque in order to enlarge the coronary lumen; risk of dissection or abrupt closure; risk of restenosis

STENT: treats the dissection associated with PTCA and \searrow the risk of abrupt closure; \searrow risk urgent CABG; \searrow restenosis

- **One-year clinical restenosis rate:** PTCA 30%; BMS 10-15%; DES 3-5%
 - **Clinical restenosis:** during the first 6-9 months post-PCI
- **DES:** \searrow restenosis and \searrow reintervention; \nearrow very late stent thrombosis (> 1 year) (risk markedly decreased with new generation DES)
 - **New generation DES:** thin-strut platform; limus-based antiproliferative drug; polymer with improved biocompatibility; improved safety compared to early-generation DES; should be considered by default in all clinical conditions and lesion subsets

BALLOON ANGIOPLASTY



PREFER DES	CONSIDER BMS
<ul style="list-style-type: none"> • LMCA • Small vessels (< 2.5 mm diameter) • Long lesion (> 20 mm) • DM • In-stent restenosis • Bifurcation • Vein graft • Chronic total occlusion 	<ul style="list-style-type: none"> • Dual antiplatelet therapy for 3-6 months impossible • Probable surgery < 6 months • Bleeding risk • Anticoagulation (Warfarin or DOAC) required

FFR (Fractional flow reserve): to determine whether an intermediate stenosis (50-70%) is hemodynamically significant

> Quantify the trans-stenotic pressure gradient

> ★ **FAME:** angioplasty guided by fractional flow reserve (FFR) determination associated with improvement of primary outcome (death; MI; reintervention)

IVUS (Intravascular ultrasound): **A)** Determines the severity of a stenosis on the LMCA; **B)** Determines the mechanism of stent restenosis or thrombosis; **C)** Guidance during complex PCI; **D)** Follow-up of cardiac allograft vasculopathy

MANUAL ASPIRATION THROMBECTOMY: aspiration of intra-coronary thrombus; ↘ distal embolism (no benefit in ★ TASTE and ★ TOTAL)

ROTATIONAL ATERECTOMY: Grinding of calcified atherosclerotic plaque; facilitates passage and deployment of the balloon and stent; risk of coronary perforation

SPECIFIC LESIONS

IN-STENT RESTENOSIS: DES implantation or drug-coated balloons; intracoronary imaging

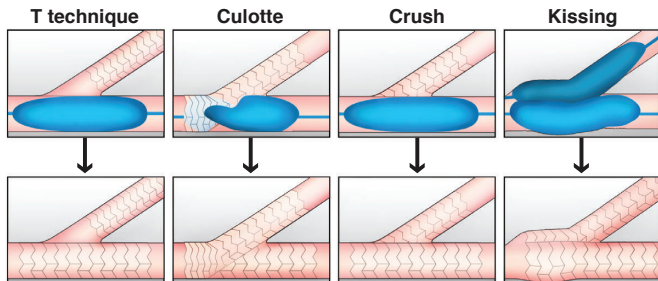
CHRONIC TOTAL OCCLUSION (CTO): revascularization in the presence of significant viability and a significant ischemic territory

> **Percutaneous revascularization:** complex technique via an antegrade approach (± subintimal dissection and re-entry) and/or retrograde approach (via collateral pathways)

PCI ON VEIN GRAFT: ↗ risk of periprocedural MI and no-reflow (atheroembolism); use an embolic protection device

BIFURCATION: 2 strategies

- PCI with stent in the main vessel only (angioplasty and/or stent in the branch if necessary)
(★ Nordic-Baltic Study IV and ★ TRYTON)
- PCI with stenting of both vessels (especially if complex bifurcation with large branch and significant risk of occlusion); terminate the operation with simultaneous inflation of a balloon in each vessel ("kissing")



LEFT MAIN CORONARY ARTERY: percutaneous revascularization possible if low risk of procedural complications (proximal LMCA; SYNTAX ≤ 32) or high surgical risk

COMPLICATIONS OF PCI**RISK OF COMPLICATIONS DURING PCI ACCORDING TO THE TYPE OF LESION**

TYPE I: Low risk	<ol style="list-style-type: none"> Patent Lesion Does not meet the criteria for a type C lesion
TYPE II	<ol style="list-style-type: none"> Patent Lesion Meets one of the criteria of a type C lesion <ul style="list-style-type: none"> Diffuse lesion (> 20 mm long) Severe proximal tortuosities Extreme angle (> 90°) Impossible to protect a major branch Vein graft with friable lesions
TYPE III	<ul style="list-style-type: none"> Occluded lesion Does not meet the criteria for a type C lesion
TYPE IV: High risk	<ul style="list-style-type: none"> Occluded lesion Meets one of the criteria of a type C lesion

COMPLICATIONS: Death (0.7% elective PCI); MI; Stroke (0.2%); TIA; Vascular access site complication; Coronary perforation (\pm tamponade); Coronary dissection (abrupt closure); No-reflow (\searrow antegrade flow in the absence of epicardial stenosis secondary to distal microembolism / vasospasm / endothelial dysfunction; management with Adenosine or intracoronary Verapamil or GPIIb/IIIa inhibitors); Branch occlusion; Urgent CABG (0.4%); ARF; Hemorrhage

- **Femoral or radial access complications:** ➤ Chapter 1 - Coronary angiography
- **Post-coronary angiography ARF:** ➤ Chapter 1 - Coronary angiography

EARLY CHEST PAIN POST-PCI: Stent thrombosis; Residual dissection / Abrupt closure; No reflow; Distal embolism; Branch occlusion

STENT THROMBOSIS: 1% at 1 year; Mortality 20-45%

- **BMS: during first 30 days** (rare after 30 days due to complete neo-endothelialization) +
- **DES: can occur after 1 year** (very late thrombosis due to incomplete neo-endothelialization); decreased risk with new generation DES +
- **Risk factors:** acute myocardial infarction; Nonadherence with P2Y₁₂ inhibitor; Resistance to Clopidogrel; DM; Long segment; Small vessels (diameter < 2.5 mm); Bifurcation; Incomplete stent apposition; Dissection at the stent margin; Overlapping stents
- **Treatment:** emergency PCI; Prasugrel or Ticagrelor; IVUS or OCT to detect mechanical problems

ADJUVANT TREATMENT - ELECTIVE PCI

► Chapter 1 - Coronary angiography

ASA: 325 mg then 80 mg qd (long term)

CLOPIDOGREL: 600 mg loading dose for elective stenting (★ ARMYDA-2) then 75 mg qd

- **BMS with bleeding risk:** Clopidogrel for a **minimum of 2-4 weeks**
- **DES:** dual antiplatelet therapy for a minimum of **6 months** (★ ISAR-SAFE)
 - Strict minimum of 3-6 months with new generation DES
 - ★ **DAPT:** 30 months of DAPT (vs 12 months) associated with ↘ stent thrombosis and MACCE but ↗ moderate or severe bleeding
 - **Prolonged dual antiplatelet therapy:** consider in the presence of a high risk of stent thrombosis (according to anatomy / procedure) or if late stent thrombosis would have major consequences (LMCA; bifurcation; ostium...)

GP1Ib/IIIA INHIBITORS: at the interventional cardiologist's discretion

UNFRACTIONATED HEPARIN: A) Procedure without GP1Ib/IIIA inhibitors: 70-100 U/kg targeting ACT 250-300 s (HemoTec) or 300-350 s (Hemochron); **B)** Procedure with GP1Ib/IIIA inhibitors: 50-70 IU/kg targeting ACT 200-250 s

STATIN PRE-PCI ↘ risk of periprocedural MI (★ ARMYDA; ★ NAPLES II)

2.9/ REVASCULARIZATION - SURGERY

ASSESSMENT OF PERIOPERATIVE RISK

STS SCORE: in-hospital or 30-day mortality, and in-hospital morbidity
/ <http://riskcalc.sts.org>

EUROSCORE II: in-hospital mortality / www.euroscore.org

ADJUVANT TREATMENT

ASA: for all patients (to protect graft patency)

P2Y₁₂ INHIBITORS: Stop Clopidogrel and Ticagrelor > 5 days pre-op; Stop Prasugrel > 7 days preop

GP1Ib/IIIA INHIBITORS: Stop Eptifibatide / Tirofiban 2-4 h pre-op; Stop Abciximab > 12 h pre-op

STATIN: for all patients

ACE INHIBITORS: for all patients (start postoperatively when hemodynamic stability is achieved)

BB: > 24h pre-op (in the absence of contraindication) to prevent perioperative AF (continue post-op)

GLYCEMIC CONTROL: target perioperative blood glucose < 10 mmol/L

ASSESSMENT OF CAROTID ARTERIES

CAROTID DOPPLER IN HIGH-RISK PATIENTS: > 65 years; LMCA; PAD; History of TIA - stroke; HTN; Smoking; DM

INDICATIONS FOR PRE-CABG REVASCULARIZATION (angioplasty / stent or endarterectomy)

- a) History of TIA or stroke with 50-99% stenosis (class IIa recommendation)
- b) Severe bilateral stenoses (70-99%) or severe unilateral stenosis (70-99%) with contralateral occlusion (class IIb recommendation)
 - > Note: diverging indications according to the various guidelines
 - > Assessment on an individual basis by a multidisciplinary team including a neurologist

COMPLICATIONS

COMPLICATIONS: Death; Stroke (micro- or macroembolism; hypoperfusion); Cardiogenic shock; Tamponade (often localized over the RA); post-CPB cognitive deficits; ARF; post-CPB SIRS; Hemorrhage; Re-exploration; Prolonged mechanical ventilation; Sternal osteomyelitis / Mediastinitis; Perioperative myocardial infarction; AF; Pulmonary complications (ARDS; Pneumonia; Atelectasis; Phrenic nerve palsy); Intestinal ischemia

MEDIASTINITIS / STERNAL INFECTION

- > **Risk factors:** DM; Obesity; COPD; Prolonged CPB; REDO; Prolonged intubation; Repeat surgical exploration
- > **Management:** Antibiotics; Surgical debridement; Reconstruction (pectoralis muscle flap); VAC; Sternal plate

VEIN GRAFT: Early occlusion rate (before discharge from hospital): 10%; 1-year occlusion rate: 25%; **10-year occlusion rate: 50%**

- > **Arterial bypass graft: 10-year patency rate > 90%**

POSTOPERATIVE ATRIAL FIBRILLATION

0-5 days post-op; Frequently resolves spontaneously in 6-12 weeks

PROPHYLAXIS: BB (1st choice); Amiodarone if BB contraindicated (400 mg PO bid x 6 days preop and 6 days post-op)

- > **Other options:** Sotalol; IV magnesium (1.5 g IV daily for 4 days post-op); Atrial overdrive; Colchicine (★ COPPS-POAF)

MANAGEMENT: rate control or rhythm control according to symptoms; anticoagulation if AF > 48 h; review treatment at 12 weeks

MINIMALLY INVASIVE SURGERY

BEATING HEART (OFF-PUMP): requires sternotomy with cardiac stabilization device; theoretically avoids the disadvantages of CPB and clamping of the ascending aorta

- > **No demonstrated benefit** to date (★ ROOBY, ★ GOPCABE, ★ CORONARY)

MIDCAB: left anterior mini-thoracotomy; beating heart internal mammary artery bypass graft to LAD; ventilation of only one lung

- > **Hybrid procedure:** LIMA to LAD; PCI of other vessels; avoids sternotomy and clamping of the aorta

ROBOTIC TOTAL ENDOSCOPIC BYPASS GRAFT: with femoro-femoral CPB

2.10/ PRINZMETAL ANGINA (VASOSPASTIC ANGINA)

Severe angina at rest with transient ST elevation

- Worse between midnight and 8:00 am
- **Risk factors:** Smoking; Migraine; Raynaud; 5-fluorouracil; Cyclophosphamide; Hyperventilation; Cold

COMPLICATIONS: MI; VT; VF; AV block; Asystole; Sudden death

STRESS TEST: 1/3 negative; 1/3 with ST elevation; 1/3 with ST depression

CORONARY ANGIOGRAPHY: Coronary spasm; RCA > LAD; Multiple spontaneous spasms on multiples vessels possible

➤ Provocation test rarely performed

- **Ergonovine provocation test:** 0.05 to 0.2 mg IV
- **Acetylcholine provocation test:** 10-25-50-100 µg intracoronary; focal spasm during Prinzmetal angina

MANAGEMENT: Smoking cessation; CCB (combination of dihydropyridine and nondihydropyridine PRN); Nitrates; Prazosin (alpha-blocking agent) and Nicorandil if necessary; Avoid nonselective BB (risk of unopposed alpha stimulation); Avoid ASA (inhibits prostacyclin synthesis); PCI if associated stenosis; Mg²⁺ supplement; Statins may be beneficial; Defibrillator for secondary prevention (especially if ischemia persists despite treatment)

2.11/ CARDIAC SYNDROME X

More or less typical retrosternal chest pain with ischemia documented on noninvasive test (ST depression and/or perfusion abnormality) in the absence of any significant epicardial CAD

Associated with increased **CARDIOVASCULAR RISK**

MECHANISM: probable microvascular endothelial dysfunction with decreased vasodilatation reserve; ± hypersensitivity to pain +

- 40-50% of the resistance to coronary flow is derived from the microvasculature; an insufficient vasodilatation reserve decreases coronary perfusion on exertion +

MANAGEMENT: ACE inhibitors and Statins (improve endothelial dysfunction); Nitrates; BB; CCB; Treatment of risk factors; Regular exercise

- **Persistent retrosternal chest pain:** Nicorandil; Imipramine or Amitriptyline; Aminophylline; Neurostimulation (spinal cord); External counterpulsation; Psycho-intervention...

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Heart failure

03

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3.1/ HEART FAILURE: ASSESSMENT

DEFINITION: Complex clinical syndrome secondary to a functional or structural abnormality of the heart which impairs the capacity of the ventricle to eject blood (and perfuse tissues) or to be adequately filled

➤ This clinical syndrome leads to typical symptoms and signs

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SYSTOLIC HEART FAILURE	HEART FAILURE WITH PRESERVED LVEF
1. Typical symptoms 2. Typical signs 3. \searrow LVEF	1. Typical symptoms 2. Typical signs 3. Normal or slightly decreased LVEF; non-dilated LV 4. Structural heart disease (LVH; LAH) and/or diastolic dysfunction

LVEF = stroke volume (end-diastolic volume – end-systolic volume) / end-diastolic volume

➤ When LVEF is decreased: stroke volume is maintained by increasing end-diastolic volume (eccentric LVH)

SYMPTOMS	SIGNS
<ul style="list-style-type: none"> Dyspnea Orthopnea PND (1-2 h after going to bed; resolution in 15-30 min) \searrow Exercise tolerance Tiredness Lower limb edema Peripheral edema Nocturnal cough Wheezing Weight gain Loss of appetite RUQ pain Nocturia 	<ul style="list-style-type: none"> Cachexia Hypotension; OH; Narrow pulse pressure Pulsus alternans; \searrow Pulse amplitude Tachycardia Tachypnea Cheyne-Stokes breathing JVD ; HJ reflux Lateralized and widened apex Left parasternal heave / Signs of PHT Decreased S1 S3 - S4 (\pm palpable) AV valve regurgitation Crackles Wheezing Signs of pleural effusion Hepatomegaly (\pm pulsatile) Peripheral edema (leg edema; scrotum; presacral; ascites) Cold extremities Confusion / Decreased level of consciousness

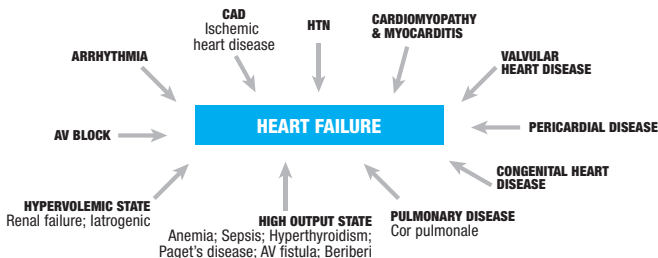
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NYHA FUNCTIONAL CLASS

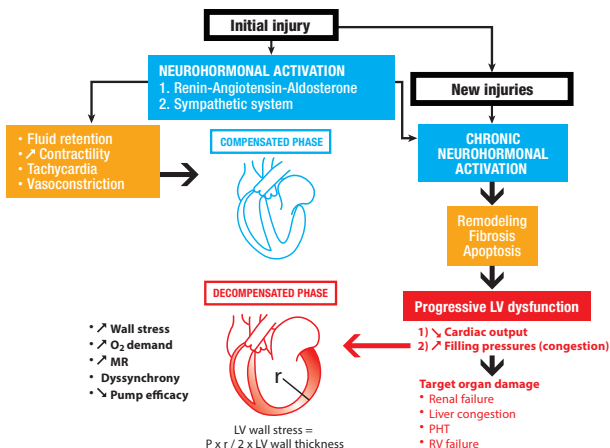
NYHA I	No limitation in ordinary physical activity (no tiredness, dyspnea or palpitations)	≥ 7 METs <ul style="list-style-type: none"> Climbing one flight of stairs with a bag of groceries Shoveling snow Bicycling; Skiing; Jogging/walking (8 kph)
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NYHA II	Slight limitation during physical activity; ordinary physical activity causes symptoms (tiredness, dyspnea, palpitations)	5-7 METs <ul style="list-style-type: none"> • Climbing one flight of stairs without stopping • Walking briskly on level ground (6.5 kph) • Gardening; Dancing
NYHA III	Marked limitation during physical activity; comfortable at rest; less than ordinary activity causes symptoms (tiredness, dyspnea, palpitations)	2-5 METs <ul style="list-style-type: none"> • Showering without a break • Getting dressed without a break • Walking briskly on level ground (4 kph) • Making a bed • Bowling; Golf
NYHA IV	Inability to carry on any physical activity without discomfort \pm symptoms at rest	< 2 METs <ul style="list-style-type: none"> • Unable to perform the activities of NYHA III

ETIOLOGIES



PATHOPHYSIOLOGY



ASSESSMENT

WORK-UP: CBC; Electrolytes (including $\text{Ca}^{2+}/\text{Mg}^{2+}$); Creatinine - BUN; LFTs; Blood glucose; HbA1c; TSH; Urinalysis; Lipids

- **If necessary:** CK; Iron assessment; HIV; ANA; RF; Urine metanephrines; SPEP - UPEP; Uric acid; CRP; Troponin; Polysomnography

ECG: Sinus tachycardia; arrhythmia (AF; PVCs; NSVT); Conduction disorder / LBBB; LVH; LAH; Q waves; ischemia; low voltage QRS

- **AV block:** Drug-induced; myocardial infarction; myocarditis; sarcoidosis; familial cardiomyopathy (LMNA; SCN5A); Lyme disease

CXR: prominent hila; Kerley B lines (fine horizontal linear opacities extending to the pleura); peribronchial edema; interstitial / alveolar edema; redistribution to apices; pleural effusion; fluid in the fissure; cardiomegaly; other cause of dyspnea

TTE (± CONTRAST): chamber dimensions; LVH; systolic and diastolic function; LVEF (Simpson); valves; PAP; thrombus; cardiac output (LVOT VTI)

RADIONUCLIDE VENTRICULOGRAPHY: LVEF; RVEF

CARDIAC MRI: cardiac structure and function; LVEF; tissue characterization; evaluation of cardiomyopathy / myocarditis

CORONARY ANGIOGRAPHY (± FFR): rule out significant CAD

- **Noninvasive evaluation** (MIBI-P; stress echocardiography; coronary CT angiography) possible if few risk factors / low pre-test probability / low impact of the result on management

STRESS TEST / 6MWT / VO_2MAX : **A)** Objective evaluation of functional class; **B)** Rule out ischemia; **C)** Pre-transplant (VO_2max); **D)** Prescription of exercise; **E)** Prognosis; **F)** Distinguish cardiac from pulmonary cause

- **$\text{VO}_2\text{max} < 12 \text{ mL O}_2/\text{kg}/\text{min}$** associated with poorer survival than in patients with a heart transplant +
- **6MWT:** normal $> 600 \text{ m}$; $< 350 \text{ m}$ roughly equivalent to NYHA III

BIOPSY: ➤➤ Chapter 5

BNP: released by the failing heart or in response to hemodynamic stress; reflects wall stress and filling pressures

- Increases with age; decreases with obesity
- **DDx** ⚡: CRF; arrhythmia; ACS; pulmonary embolism; severe COPD / PHT; sepsis; cirrhosis
- **Indications:** **A)** Identify the cause of dyspnea (cardiac versus non-cardiac); **B)** Prognosis
 - BNP-guided management of heart failure remains controversial; studies report divergent results

ACUTE HEART FAILURE UNLIKELY	NT-proBNP < 300 pg/mL (NPV 98 %)	BNP < 100 pg/mL
PROBABLE ACUTE HEART FAILURE	NT-proBNP > 450 pg/mL (< 50 years) > 900 pg/mL (50-75 years) > 1800 pg/mL (> 75 years)	BNP > 500 pg/mL

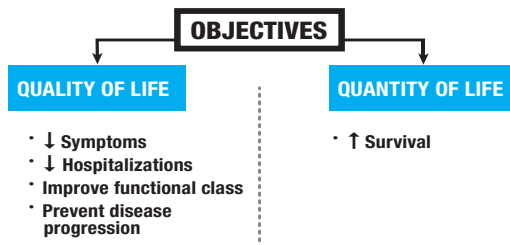
- **Variation:** a change of $> 30\%$ in BNP level should call for more intensive follow-up / treatment

SEATTLE HEART FAILURE MODEL: <http://depts.washington.edu/shfm>

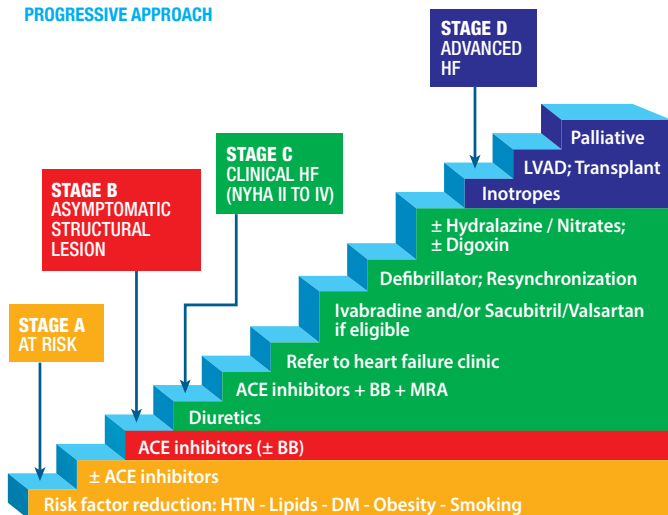
HEART FAILURE SURVIVAL SCORE

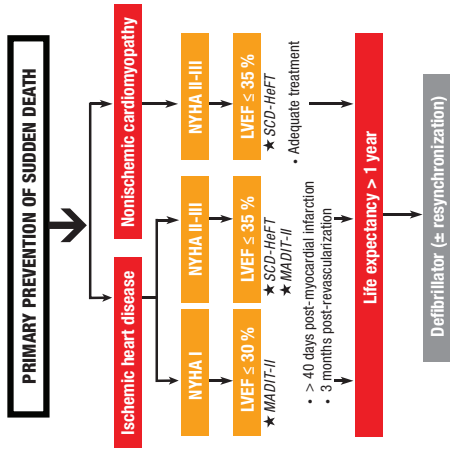
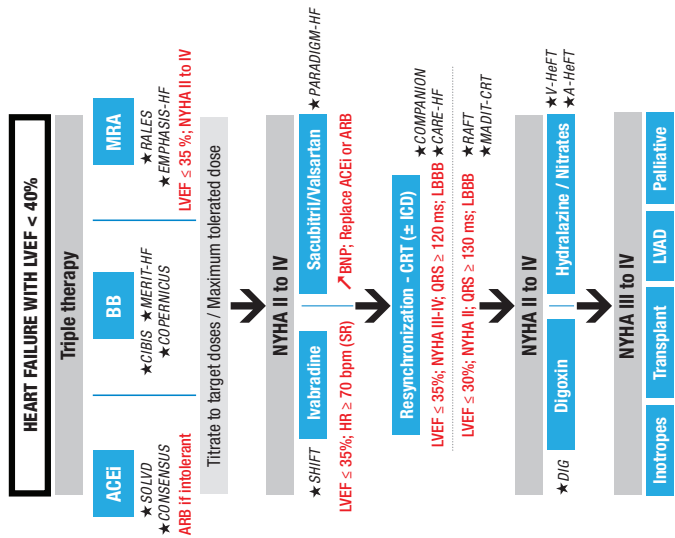
PROGNOSTIC FACTORS: Demographics; Etiology; Comorbidities; NYHA; Hemodynamics (LVEF; PAP; Wedge; Cardiac index; Transpulmonary gradient); Exercise stress test (BP; 6MWT; VO_{2max} ; Anaerobic threshold; Ve/VCO_2 slope > 35); Anemia; Hyponatremia; QRS duration; BNP; Troponin...

3.2/ SYSTOLIC HEART FAILURE: MANAGEMENT



PROGRESSIVE APPROACH





	INITIAL DOSE (mg)	TARGET DOSE (mg) (to be reached whenever possible)
ACE INHIBITORS - ANGIOTENSIN-CONVERTING ENZYME INHIBITORS		
Captopril	6.25 tid	50 tid
Enalapril	1.25 bid	10-20 bid
Lisinopril	2.5 qd	20-40 qd
Ramipril	1.25 bid	5 bid
Perindopril	2.5 qd (2 qd in Canada)	10 qd (8 qd in Canada)
Trandolapril	0.5 qd	4 qd
BB - BETA-BLOCKERS		
Bisoprolol	1.25 qd	10 qd
Carvedilol	3.125 bid	25-50 bid
Metoprolol succinate XL	12.5-25 qd	200 qd
ARB - ANGIOTENSIN RECEPTOR BLOCKERS		
Candesartan	4 qd	32 qd
Valsartan	20-40 bid	160 bid
NEPRILYSIN INHIBITOR		
Sacubitril / Valsartan	50 (24/26) - 100 (49/51) mg bid	200 (97/103) mg bid
I_f CHANNEL INHIBITOR		
Ivabradine	5 bid	7.5 bid
LOOP DIURETICS		
Furosemide	20-40 qd or bid (adjusted to renal function)	max 600 /24h
Bumetanide	0.5-1 qd or bid	max 10 /24h
MRA - MINERALOCORTICOID RECEPTOR ANTAGONISTS		
Spironolactone or Eplerenone	Eplerenone CrCl > 50 mL/min: 25 mg qd; CrCl 30-49 mL/min: 25 mg every 2 days Spironolactone CrCl > 50 mL/min: 12.5 to 25 mg qd; CrCl 30-49 mL/min: 12.5 mg qd or every 2 days	Eplerenone CrCl > 50 mL/min: 50 mg qd; CrCl 30-49 mL/min: 25 mg qd Spironolactone CrCl > 50 mL/min: 25 mg qd or bid; CrCl 30-49 mL/min: 12.5 to 25 mg qd
THIAZIDE DIURETICS		
Hydrochlorothiazide	25 qd ou bid	max 200 /24h
Metolazone	2.5-5 qd	max 20 /24h
Indapamide	2.5 qd	max 5 /24h
DIGOXIN		
Digoxin	0.125 Adjusted to renal function Total loading dose of 1 mg PO per 24 h in 4 doses divided on the 1 st day when rapid effect is required; adjusted to renal function	Plasma target: 0.5 to 0.9 ng/mL (1 week after titration)
HYDRALAZINE / NITRATES		
Hydralazine / Nitrates	Hydralazine: 10-25 tid Isosorbide dinitrate: 10 tid	Hydralazine: 75 tid Isosorbide dinitrate: 40 tid

ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS

↘ Mortality; ↘ Hospitalization; Stabilizes remodeling; ↘ Symptoms

STUDIES: ★ CONSENSUS - ★ SOLVD; ★ SOLVD-Prevention (asymptomatic ↘ LVEF - NYHA I); ★ SAVE - ★ AIRE - ★ TRACE (myocardial infarction with heart failure and/or ↘ LVEF); ★ ATLAS (low-dose vs high-dose Lisinopril)

ADVERSE EFFECTS: ARF; hyperkalemia; hypotension; cough (secondary to ↗ bradykinins); angioedema

CONTRAINDICATIONS: angioedema; bilateral renal artery stenosis; pregnancy

➤ **Caution:** creatinine > 221 µmol/L (> 2.5 mg/dL) or GFR < 30 mL/min/1.73m²; hyperkalemia > 5.5 mmol/L; SBP < 90 mmHg

• < 30% rise in creatinine or elevation of K⁺ up to 5.5 mmol/L is acceptable

+

➤ **Follow-up:** assessment 1 week after titration (creatinine; BUN; electrolytes)

BETA-BLOCKERS (BB)

↘ Mortality; ↘ Hospitalization; ↘ Remodeling; ↘ Symptoms

STUDIES: ★ CIBIS (Bisoprolol) - ★ COPERNICUS (Carvedilol) - ★ MERIT-HF (Metoprolol succinate XL); ★ SENIORS (Nebivolol; > 70 years); ★ COMET (Carvedilol vs Metoprolol tartrate); ★ B-CONVINCED (BB continued in the presence of decompensation); ★ CAPRICORN - ★ BEAT (post-myocardial infarction)

ADVERSE EFFECTS: decompensated heart failure; bronchospasm; bradycardia / block; hypotension; tiredness; depression; nightmares; erectile dysfunction; glucose intolerance

CONTRAINDICATIONS: active decompensated heart failure (continue BB if already used predecompensation); shock - hypoperfusion; asthma; 2nd or 3rd degree AV block; severe PAD (ischemia at rest)

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➤ **Treat congestion before initiating a BB; target euvolemia**

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➤ **Titrate the dose every 2 weeks**

➤ **Caution:** HR < 60 bpm; recent decompensation; NYHA IV; SBP < 90 mmHg

➤ **COPD:** favor beta-1 selective BB (Bisoprolol; Metoprolol)

MINERALOCORTICOID RECEPTOR ANTAGONISTS (MRA)

↘ Mortality; ↘ Hospitalization; ↘ Symptoms

STUDIES: ★ RALES (NYHA III-IV; LVEF < 35 %); ★ EMPHASIS-HF (NYHA II; LVEF < 30 % or < 35 % with QRS > 130 ms; Recent hospitalization or ↗ BNP); ★ EPHEsus (myocardial infarction; LVEF < 40%; heart failure or DM)

ADVERSE EFFECTS: hyperkalemia; ARF; gynecomastia - impotence - ↘ libido - menstrual irregularities (Spironolactone)

CONTRAINDICATIONS: CRF (creatinine > 221 µmol/L in males or > 177 µmol/L in females or GFR < 30 mL/min); hyperkalemia > 5 mmol/L

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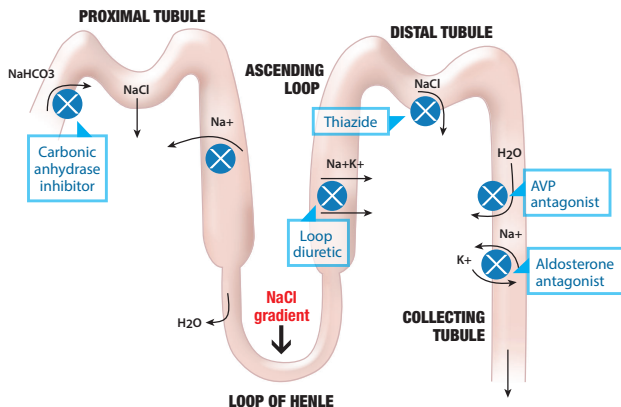
➤ Titration every 4-8 weeks

➤ **Follow-up:** assessment 1 week and 4 weeks after titration; at 8 weeks - 12 weeks; at 6 - 9 - 12 months; then every 4 months

DIURETICS

↘ Symptoms

Target dry weight; target lowest possible dose



ADVERSE EFFECTS: ARF; hypovolemia; hypokalemia; hyponatremia (thiazides); hypomagnesemia; metabolic alkalosis; hyperuricemia; ototoxicity

CAUTION: CRF; hypokalemia; hypotension

➤ **Follow-up:** assessment 1 week after titration (creatinine; BUN; electrolytes; Mg^{2+})

➤ **Target K^+** 4-5 mmol/L



	SODIUM EXCRETION	DURATION OF ACTION	COMMENTS
Loop diuretics	25 %	4-8 h (furosemide)	<ul style="list-style-type: none"> Inhibition of the ascending loop Na-K-2Cl pump Secreted into the proximal tubule (this secretion depends on renal perfusion and the bioavailability of the drug) Dose-effect response (a tubular concentration threshold must be reached to obtain an effect) Venodilator effect
Thiazides	5-10 %	6-12 h (HCTZ) 12-24 h (Metolazone)	<ul style="list-style-type: none"> Inhibition of the distal tubule Na-Cl pump Less effective when $\text{GFR} < 30 \text{ mL/min}$ ➤ clearance of free water (risk of hyponatremia); ➤ Ca^{2+} reabsorption
Mineralo-corticoid receptor antagonists	1-2 %	2-3 h	<ul style="list-style-type: none"> Inhibition of the collecting tubule Na-K pump at the site of action of aldosterone Antagonism of the harmful effects of aldosterone on the heart
Vasopressin antagonist	0 %	24 h	<ul style="list-style-type: none"> Free water diuresis (aquaretic) Action on collecting tubule (V_2 receptors) Useful in the presence of hyponatremia; no benefit in ★EVEREST

DIURETIC RESISTANCE

- **Mechanisms:** **A)** Post-sodium excretion stimulation of RAA / sympathetic systems (rebound sodium absorption); **B)** ↘ Drug absorption (edema of intestinal wall); **C)** ↘ Cardiac output (↘ renal perfusion therefore ↘ tubular secretion of the diuretic); **D)** Hypertrophy of distal tubule; **E)** ARF or cardiorenal syndrome
- **Management**
 - a) Strict water / NaCl restriction
 - b) Increase the dose of the loop diuretic or increase the frequency of administration
 - c) Addition of an mineralocorticoid receptor antagonist
 - d) Combination of loop diuretic and metolazone (temporary measure; daily assessments)
 - e) Continuous Lasix infusion (sustained sodium excretion):
 - 20-40 mg IV bolus then infusion 5-40 mg/h (400 mg/100 mL NS)
 - f) Inotropes: Dopamine (renal effect) or Dobutamine or Milrinone
 - g) Ultrafiltration: refractory patient (★UNLOAD: ↘ Hospitalization; no benefit in ★CARESS-HF); slow continuous veno-venous method

ANGIOTENSIN RECEPTOR BLOCKERS (ARB)

INDICATIONS: **A)** Intolerance to ACE inhibitors (cough; angioedema); **B)** In combination with ACE inhibitors if intolerant to mineralocorticoid receptor antagonists and persistent symptoms

STUDIES

- **Intolerance to ACE inhibitors:** ★ CHARM-Alternative (Candesartan); ↘ Cardiovascular mortality; ↘ Hospitalization
- **ARB combined with ACE inhibitors:** ★ Val-HeFT (Valsartan) - ★ CHARM-ADDED (Candesartan); ↘ Cardiovascular mortality (Candesartan); ↘ Hospitalization; ↘ Symptoms
- **Post-myocardial infarction** (with heart failure and/or ↘ LVEF): ★ VALIANT (Valsartan vs Captopril vs Combination) → Valsartan non-inferior to Captopril

NEPRILYSIN INHIBITOR

➤ Active natriuretic peptides

★ **PARADIGM-HF:** LVEF ≤ 35-40 %; NYHA II-IV; NTproBNP ≥ 600 pg/ml (or ≥ 400 pg/ml if hospitalized < 12 months); Sacubitril + Valsartan vs Enalapril → ↘ Mortality; ↘ Hospitalization; ↘ Symptoms; ➤ Hypotension; ➤ Angioedema

DOSING (SACUBITRIL/VALSARTAN): stop ACEi 36 h before; start with 50 (24/26) or 100 (49/51) mg bid; double the dose after 2-4 weeks; target dose of 200 (97/103) mg bid if tolerated

IVABRADINE

Inhibits the sinoatrial node I_f current channel

STUDIES: ★ SHIFT (LVEF ≤ 35 %; NYHA II-IV; HR ≥ 70 bpm; recent hospitalization); ↘ Hospitalization; ↘ Symptoms; ↘ Remodeling

ADVERSE EFFECTS: bradycardia; phosphenes

DIGOXIN

Inhibits the Na-K-ATPase pump: ➤ intramyocyte Ca²⁺ (positive inotropic agent); ➤ vagal tone

INDICATIONS: **A)** Persistent symptoms despite standard treatment; **B)** AF (rate control)

STUDIES: ★ DIG (NYHA II-IV; LVEF < 45 %) → ↘ Hospitalization; ↘ Symptoms

Adjustment according to renal function and serum digoxin levels

- **Target serum Digoxin level 0.5 to 0.9 ng/mL**

+

ADVERSE EFFECTS: atrial / junctional / ventricular arrhythmias (especially in the presence of hypokalemia) combined with blocks; visual disorders; confusion; GI symptoms

CONTRAINDICATIONS: CRF; bradycardia - blocks

MULTIPLE DRUG INTERACTIONS

- ↗ **Serum Digoxin levels:** Amiodarone; Verapamil; Nifedipine; Diltiazem; Quinidine; Propafenone; Captopril; Carvedilol; Spironolactone; Cyclosporine; Macrolides

HYDRALAZINE - ISOSORBIDE DINITRATE

- ↘ **Mortality in Afro-Americans;** ↘ Hospitalization; ↘ Symptoms

INDICATIONS: **A)** Intolerance to ACE inhibitors and ARB; **B)** Persistent symptoms despite BB - ACE inhibitors - MRA (**particularly in Afro-Americans**)

STUDIES: ★ V-HeFT-1 and 2; ★ A-HeFT (Afro-Americans)

ADVERSE EFFECTS: headache; hypotension; nausea; arthralgia; asymptomatic ↗ ANA; drug-induced lupus

NON-PHARMACOLOGICAL TREATMENT**SELF-SURVEILLANCE OF WEIGHT**

- Daily weight; on waking; before getting dressed; post-voiding → increase the dose of diuretics or notify if weight ↗ > 1.5-2 kg or 3-4 lbs (x 2-3 days)

SODIUM: < 2-3 g per day

FLUIDS: < 2 liters per day (especially if hyponatremia or refractory congestion)

VACCINATION: influenza (annually); pneumococcus (every 5 years)

TREATMENTS TO BE AVOIDED: **A)** Thiazolidinediones; **B)** Non-dihydropyridine CCBs; **C)** NSAIDs; **D)** Certain AAD: Dronedarone (★ ANDROMEDA); Class I AAD (★ CAST); **E)** Alpha-blockers

EXERCISE

- ★ **HF-ACTION** → improves symptoms and functional capacity

Regular isotonic exercise (walking; stationary bike) after stress test (rule out ischemia - arrhythmia)

- **Prescription:** 3-5 times a week; 30-45 min; **60-70% of peak heart rate** (or peak $\dot{V}O_2$) or **4-5-6/10 on Borg's scale** (▶▶ Chapter 9)

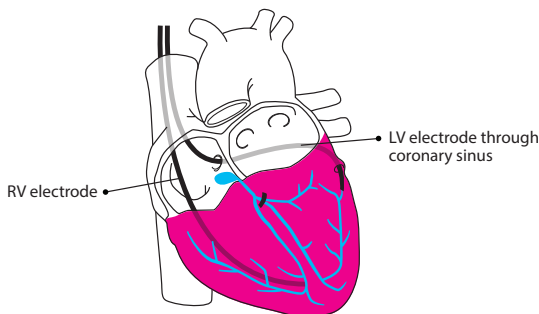
IMPLANTABLE CARDIAC DEFIBRILLATOR (ICD)

SECONDARY PREVENTION: defibrillator indicated

PRIMARY PREVENTION

- **Studies:** ★ SCD-HeFT (nonischemic cardiomyopathy or ischemic heart disease; NYHA II-III; LVEF ≤ 35% [mean = 25%]) and ★ MADIT-II (ischemic heart disease; LVEF ≤ 30%; NYHA I-III) → ↘ mortality
- **Avoid in NYHA IV (except when the patient is a candidate for transplant or mechanical support) due to poor prognosis and death predominantly secondary to progressive heart failure**

CARDIAC RESYNCHRONIZATION THERAPY (CRT)



INDICATIONS

<ul style="list-style-type: none"> ✓ AMBULANT, NYHA III OR IV ✓ LVEF $\leq 35\%$ ✓ LBBB - QRS ≥ 120 MS ✓ SINUS RHYTHM ✓ LIFE EXPECTANCY > 1 YEAR 	<ul style="list-style-type: none"> ✓ NYHA II ✓ LVEF $\leq 30\%$ ✓ LBBB - QRS $\geq 120-130$ MS ✓ SINUS RHYTHM ✓ LIFE EXPECTANCY > 1 YEAR
STUDIES: ★ CARE-HF - COMPANION ↘ Mortality; ↘ Hospitalization; ↘ Symptoms; Reverse remodeling	STUDIES: ★ RAFT - MADIT-CRT ↘ Mortality (★ RAFT); ↘ Hospitalization; ↘ Symptoms; Reverse remodeling

UNCERTAIN BENEFICIAL EFFECTS OF RESYNCHRONIZATION

- a) **Permanent AF with above indications** (consider AV node blocking agents or AV node ablation to force resynchronization)
- b) **Patient with systolic dysfunction and frequent RV pacing** (consider resynchronization if significant RV pacing $> 40\%$)

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PROCEDURAL SUCCESS: 90 %

- > Minithoracotomy approach with epicardial lead PRN
- > **Complications (14% in ★ RAFT):** pneumothorax; pocket hematoma; pocket infection; lead migration; coronary sinus perforation / dissection (1%)

PARAMETERS INFLUENCING THE RESPONSE TO RESYNCHRONIZATION: % biventricular pacing; baseline degree of asynchrony (QRS ≥ 150 ms); lead position (target = basal lateral branch of CS); lead pacing scar tissue; ischemic heart disease \ll nonischemic cardiomyopathy; CRT programming (AV delay; VV delay)

- > **Non-responders:** 30 %

ATRIAL FIBRILLATION

RATE CONTROL: non-inferior to rhythm control (★ AF-CHF)

+

- > **A)** BB; **B)** Digoxin; **C)** Amiodarone to control HR as necessary (patient should be anticoagulated for 1 month because of the risk of CCV); **D)** AV node ablation + PPM; consider resynchronization

RHYTHM CONTROL: patients with severe symptoms or reversible cause / precipitating factor

- > **A)** ECV; **B)** Amiodarone or Dofetilide; **C)** \pm PV isolation (benefit in ★ PABA-CHF and ★ AATAC-AF)

WARFARIN - ANTICOAGULATION

INDICATIONS: **A)** AF; **B)** Thrombus; **C)** History of thromboembolic disease

No benefit in ★ WARCEF study (LVEF < 35% in SR; for thromboembolic primary prevention)

SLEEP-DISORDERED BREATHING

CENTRAL SLEEP APNEA - CHEYNE-STOKES (40%): hyperventilation followed by apnea (≥ 10 s with no ventilatory effort); **associated with pulmonary congestion**; independent risk factor of mortality

- **Diagnosis:** Polysomnography
- **Treatment:** Optimize management of heart failure; CPAP (no benefit in ★ CANPAP study); Adaptive servo-ventilation associated with ↗ mortality in ★ SERVE-HF

OBSTRUCTIVE SLEEP APNEA (10%): Leads to hypoxemia / hypercapnia / intermittent sympathetic stimulation

- Look for obesity / ↗ neck circumference; snoring; daytime sleepiness; apneas
- **Complications:** refractory HTN; nocturnal HTN; PHT; arrhythmias
- **Diagnosis:** Polysomnography (screening with nocturnal saturimetry)
- **Treatment:** Weight loss; CPAP

ANEMIA

Multifactorial

TREATMENT: Transfusions; IV iron (★ FAIR-HF; ★ CONFIRM HF); no benefit for EPO (★ RED-HF)

ISCHEMIC LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

REVASCLARIZATION: possible benefit in the presence of significant viability; highly controversial topic (mixed results of ★ STICH study; ★ ISCHEMIA study ongoing)

FUNCTIONAL MITRAL REGURGITATION

Carpentier I and IIb mechanisms; maintains systolic dysfunction (which maintains MR)

MVR OR MITRAL ANNULOPLASTY: possible improvement in functional class; associated with reverse remodeling; no convincing data on survival; MVR possibly superior (★ CTSN)

- Consider in severe secondary MR with: CABG or concomitant AVR (class IIa recommendation) or refractory NYHA III - IV (class IIb recommendation)

MITRACLIP: consider in the presence of significant MR with refractory symptoms in a patient who is not a candidate for surgery

3.3/ DIASTOLIC HEART FAILURE (preserved LVEF)

Secondary to abnormal active relaxation and/or ↗ passive rigidity

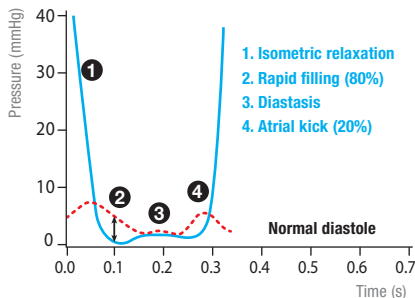
50% of patients with heart failure

ALL-CAUSE MORTALITY similar to that of heart failure with ↘ LVEF

- Mortality is mostly due to non-cardiovascular causes

RISK FACTORS: Age; Female; HTN; LVH; Ischemia; DM; Obesity; RCM; HCM

FACTORS ASSOCIATED WITH DECOMPENSATION: uncontrolled / labile HTN; AF; Ischemia; Volume overload; Extracardiac cause

**DIASTOLIC DYSFUNCTION**

Abnormal relaxation and/or ↑ passive rigidity

↑ Filling pressures

↑ LA pressure

ETIOLOGIES OF**↓ RELAXATION VELOCITY**

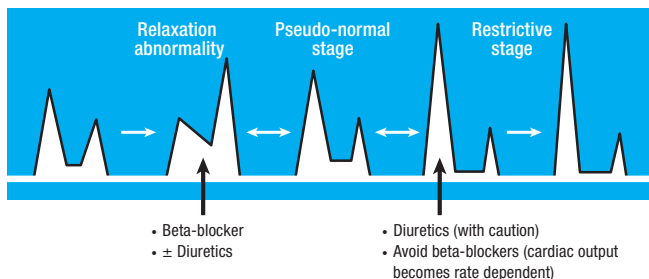
- ↑ LV afterload
- Ischemia
- Age
- Systolic dysfunction (↓ recoil)
- LVH

TTE: LVH - concentric remodeling; diastolic pattern; filling pressures; LA dilatation; PAP; RV function; Rule out pericardial disease

- ➤ **Filling pressures:** $E/e' > 15$; E/A inversion with Valsalva; diastolic dominance (PV outflow); prolonged reversal of flow in PV during atrial kick; LA dilatation; PHT

STRESS TEST: Rule out exaggerated hypertensive response (which exacerbates diastolic dysfunction); Rule out chronotropic incompetence

BNP: less sensitive than in systolic heart failure

MANAGEMENT**No treatment proven to decrease morbidity or mortality**

- **No benefit in:** ★ CHARM-Preserved - ★ PEP-CHF - ★ I-Preserve - ★ TOPCAT - ★ NEAT-HFpEF

DIURETICS: symptoms / congestion control

RISK FACTOR REDUCTION: CAD; HTN (rule out renovascular syndrome in the presence of refractory HTN)

REVASCUARIZATION: if significant ischemia / symptoms

RATE CONTROL during AF (± rhythm control)

CONSIDER: ACE inhibitor or ARB; BB; MRA

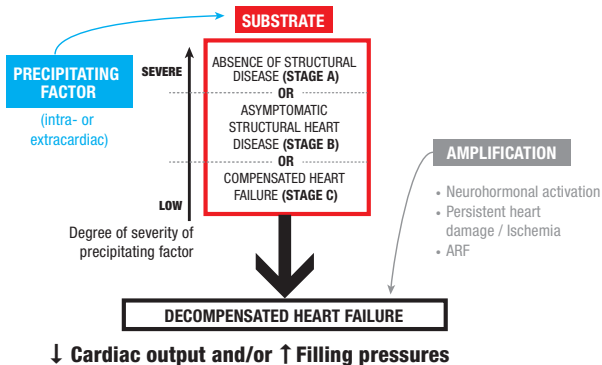
3.4/ DECOMPENSATED HEART FAILURE

Acute or subacute onset or modification of symptoms and signs of heart failure

Decompensated chronic heart failure (80%) vs *de novo* heart failure (20%)

50% of patients have preserved LVEF

PATHOPHYSIOLOGY



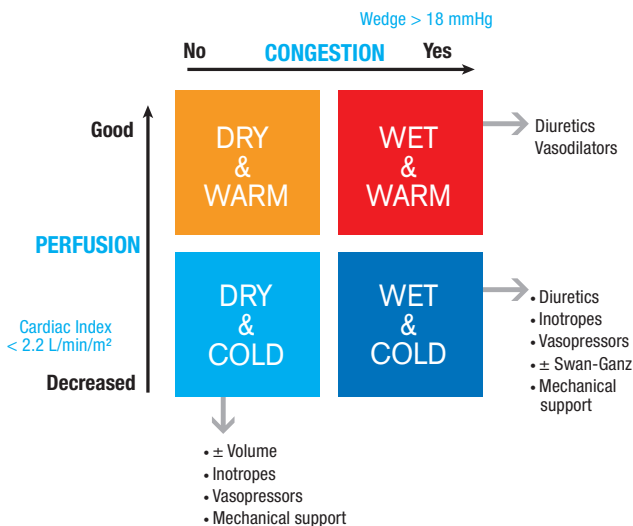
VARIOUS SCENARIOS

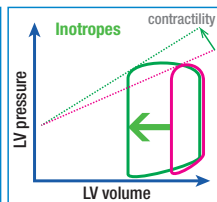
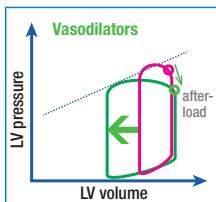
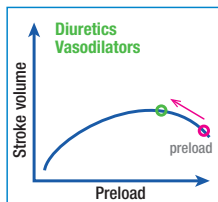
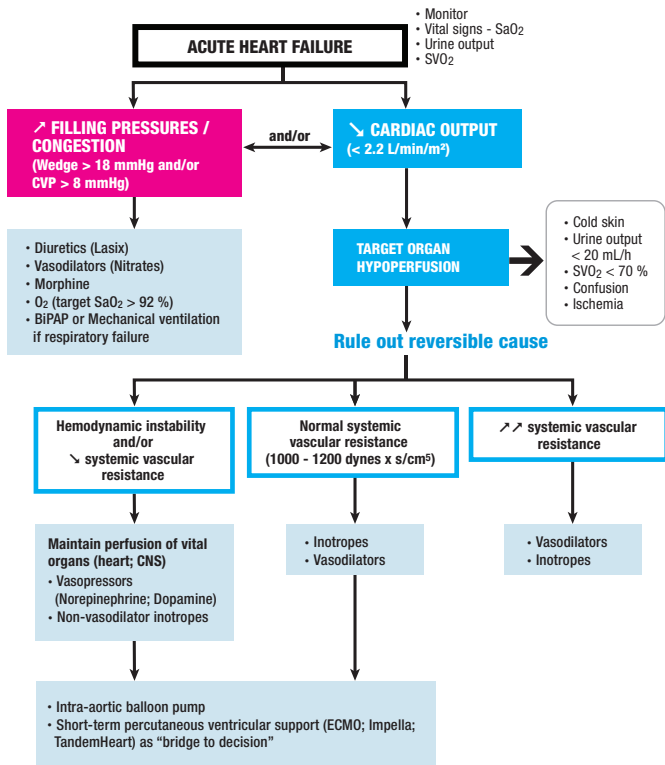
TAS > 160; ACUTE PULMONARY EDEMA	NORMAL BP	HYPOTENSION (SBP < 90)
<ul style="list-style-type: none"> • LVEF often preserved • Acute pulmonary edema • Treatment: Vasodilators; Diuretics; BiPAP; Rule out renal artery stenosis 	<ul style="list-style-type: none"> • Systemic congestion • Subacute (often decompensated chronic heart failure) • Treatment: Diuretics; ± Vasodilators 	<ul style="list-style-type: none"> • Low output • Renal hypoperfusion • Treatment: Positive inotropes (Milrinone; Dobutamine); Vasopressors; Mechanical support
CARDIOGENIC SHOCK	MYOCARDIAL INFARCTION (KILLIP II OR III)	RIGHT HEART FAILURE
<ul style="list-style-type: none"> • Acute event (ACS; mechanical complication; fulminant myocarditis) • Treatment: Reperfusion; Positive inotropes; Vasopressors; IABP; Mechanical support; Surgery 	<ul style="list-style-type: none"> • Rapid onset • Resolution with treatment of ischemia • Treatment: Reperfusion; Nitrates; Ensure good coronary perfusion pressure 	<ul style="list-style-type: none"> • RV infarction; PHT; Pulmonary embolism • Hypotension / systemic congestion • Interventricular dependence: RV dilatation induces ↘ LV filling • Treatment: Diuretics; Inotropes; Reperfusion; Pulmonary vasodilators

PRECIPITATING FACTORS

ACUTE DETERIORATION	SUBACUTE DETERIORATION
<ul style="list-style-type: none"> • Tachyarrhythmia • Bradyarrhythmia - Blocks • Acute coronary syndrome / Ischemia • Mechanical complication of MI • Valvular heart disease (e.g.: ischemic MR) • Pulmonary embolism • Hypertensive crisis • Cardiac tamponade • Aortic dissection • Surgery • Hemorrhage • Endocarditis 	<ul style="list-style-type: none"> • Infection • COPD exacerbation / Asthma • ARF • Nonadherence to treatment • Nonadherence to restrictions • Drugs (NSAID; corticosteroids; Pregabalin) • Arrhythmias - Blocks • Uncontrolled HTN • Hypothyroidism / Hyperthyroidism • Alcohol - Illicit drugs • Anemia • LBBB • Progression of heart disease

MANAGEMENT





VASODILATORS		
Nitroglycerin	Dose: 10-20 µg/min up to 200 µg/min	<ul style="list-style-type: none"> • ↑ cGMP in smooth muscle cells (= vasodilatation) • Venous vasodilator (↓ filling pressures) then arterial (↓ afterload; coronary vasodilatation) • Adverse effects: Tolerance during prolonged use; Hypotension; Headache
	Standard dilution: 50 mg/250 mL D5% = 200 µg/mL	
Nitroprusside	Dose: 0.3 µg/kg/min up to 5 µg/kg/min	<ul style="list-style-type: none"> • Balanced vasodilator • Short half-life • Used for hypertensive emergency or acute MR • Adverse effects: Risk of cyanide toxicity; Hypotension
	Standard dilution: 50 mg/250 mL NS = 200 µg/mL	
Nesiritide	<ul style="list-style-type: none"> • Bolus: 2 µg/kg • Perfusion: 0.01-0.03 µg/kg/min 	<ul style="list-style-type: none"> • Recombinant BNP • Balanced vasodilator • No benefit in ★ ROSE-AHF and ★ ASCEND-HF
INOTROPES		
Dobutamine	Dose: 2-20 µg/kg/min	<ul style="list-style-type: none"> • Beta-1 and beta-2 agonist • Supplementary alpha-1 effect at higher doses (neutralizing the beta-2 vasodilator effect) • Favor to Milrinone in the presence of significant hypotension • Arrhythmogenic
	Standard dilution: 250 mg/ 100 mL D5% = 2500 µg/mL	
Dopamine	<ul style="list-style-type: none"> • Renal effect (Dopamine) < 3 µg/kg/min • Beta-1: 3-5 µg/kg/min • Alpha-1 (and Beta-1): > 5 µg/kg/min (up to 20 µg/kg/min) 	<ul style="list-style-type: none"> • Dose-dependent effect • Positive inotrope and vasopressor (vasodilator at low doses) • Norepinephrine precursor • Arrhythmogenic • ↑ Mortality in cardiogenic shock (★ SOAP II)
	Standard dilution: 400 mg / 250 mL D5% = 1600 µg/mL	
Milrinone	<ul style="list-style-type: none"> • Bolus: 25-75 µg/kg x 10-20 min (optional; avoid if hypotension) • Infusion: 0.375 - 0.75 µg/kg/min • Adjustment to GFR 	<ul style="list-style-type: none"> • Phosphodiesterase inhibitor (↑ intra-myocyte cAMP = ↑ intracellular Ca²⁺) • Risk of hypotension (vasodilator) • Caution in patients with CAD (hypotension can accentuate ischemia) • Effective despite BB • Favor if BP preserved • Less arrhythmogenic than dobutamine • No benefit in ★ OPTIME-HF study
	Standard dilution: 10 mg/100 mL D5% = 90 µg/mL	
Levosimendan	<ul style="list-style-type: none"> • Bolus: 12 µg/kg x 10 min (optional; risk of hypotension) • Infusion 0.05 - 0.2 µg/kg/min 	<ul style="list-style-type: none"> • Calcium sensitizer • Positive inotrope and vasodilator • Equivalent to Dobutamine in ★ SURVIVE

Isuprel	Dose: 0.5 to 10 µg/min	<ul style="list-style-type: none">• Beta-1 and beta-2 agonist• Prominent positive chronotropic effect• Risk of hypotension (beta-2 effect)
	Standard dilution: 1 mg / 250 mL D5% = 4 µg/mL	
VASOPRESSORS		
Norepinephrine	Dose: 0.2 -1 µg/kg/min	<ul style="list-style-type: none">• Alpha-1 agonist• Beta-1 effect (but reflex bradycardia secondary to ↗ MAP)
	Standard dilution: 4 mg / 250 mL D5% = 16 µg/mL	
Epinephrine	<ul style="list-style-type: none">• Bolus: 1 mg IV every 3-5 min (during resuscitation)• Infusion: 0.05 - 0.5 µg/kg/min	<ul style="list-style-type: none">• Alpha-1, beta-1 and beta-2 agonist• Arrhythmogenic
	Standard dilution: 5 mg / 250 mL D5% = 20 µg/mL	
Phenylephrine	Dose: 40 - 60 µg/min	<ul style="list-style-type: none">• Pure alpha-1 agonist
	Standard dilution: 10 mg / 250 mL NS = 40 µg/mL	

MONITORING: Cardiac monitoring - Regular vital signs - SaO₂ - urine output; daily weight

LMNOP: **I**V Lasix; **M**orphine if anxiety / distress (2.5-5 mg IV); **N**itrates (avoid if hypotension); **O**₂; **P**osition - PEEP

- **Diuretic:** ★ DOSE study → bolus bid equivalent to IV infusion; low-dose IV (equal to usual oral doses) equivalent to high-dose IV (2.5 x usual oral doses)
- **BiPAP:** contraindicated in the presence of hypotension; Vomiting; Impaired level of consciousness; Uncooperative patient

INOTROPES (Dobutamine; Milrinone): **indicated in the presence of peripheral hypoperfusion**

- **Adverse effects:** Hypotension (vasodilator effect); Arrhythmogenic; ↗ O₂ demand; ↗ Long-term mortality

VASOPRESSORS (Norepinephrine): indicated in the presence of severe hypotension

- **Objective:** redirect cardiac output to vital organs

- **Adverse effects:** ↗ Afterload; ↗ O₂ demand; Arrhythmogenic

SWAN-GANZ: Indications → **A**) Cardiogenic shock despite inotropes / vasopressors;

B) Patient refractory to treatment; **C**) Uncertain hemodynamic parameters (filling pressures; SVR);

D) Hemodynamic assessment prior to transplant / mechanical support

- **Hemodynamic targets**

WEDGE	CVP	BP	SVO ₂	SVR	CARDIAC INDEX
< 18 mmHg	< 8 mmHg	MAP > 60 mmHg SBP > 80 mmHg	> 70 %	1000 to 1200 dynes s / cm ⁵	> 2.2 L/min/m ²

MONITORING OF TREATMENT: improvement in symptoms / signs of congestion / peripheral perfusion; SVO₂; BP; weakness - OH; urine output; daily weight; CVP; BUN - creatinine - electrolytes

IDENTIFICATION AND TREATMENT OF REVERSIBLE CAUSES: Ischemia; Arrhythmia;

Valvular heart disease; Other precipitating factors

DISCHARGE FROM HOSPITAL: congestion resolved; **dry weight achieved;** ACE inhibitors - BB - mineralocorticoid receptor antagonist initiated; stable dose of diuretics and stable labs for > 48 h; restrictions explained; registration in specialized clinic; follow-up < 1 month (vulnerable phase)

SHORT-TERM AND MEDIUM-TERM MECHANICAL SUPPORT

OBJECTIVE: Maintain adequate target organ perfusion during acute treatment and/or while waiting for recovery and/or while waiting for heart transplant or long-term ventricular support

SHORT-TERM PERCUTANEOUS MECHANICAL SUPPORT

- **IABP:** increases cardiac output $< 10-15\%$; increases coronary perfusion; contraindicated in the presence of AR or aortic dissection
- **Impella 2.5 and 5.0 L/min:** Femoral artery → Aortic valve
- **TandemHeart:** **A)** Filling cannula: femoral vein → transseptal → LA; **B)** Ejection cannula: femoral artery
 - **Disadvantages** (Impella and TandemHeart): lower limb ischemia; cannula displacement; difficult transport
- **ECMO:** complete cardiopulmonary support
 - **Disadvantages:** anticoagulation; lower limb ischemia; incomplete LV decompression; requires qualified personnel; activation of an inflammatory cascade

MEDIUM-TERM MECHANICAL SUPPORT (LVAD OR RVAD OR PARACORPOREAL BIVAD)

Thoratec VAD; CentriMag; Abiomed BVS5000

CARDIORENAL SYNDROME

Impaired renal function associated with heart failure

MECHANISMS: **A)** Low output; **B)** Venous congestion; **C)** Medications (ACE inhibitors; ARB; contrast agents); **D)** Intravascular hypovolemia (diuretics) = activation of RAA / sympathetic systems; **E)** Underlying renal disease (HTN; DM; PAD); **F)** ➤ Intra-abdominal pressure (ascites)

RENAL PERFUSION PRESSURE = MAP - CVP

NORMAL RENAL FUNCTION	GFR > 90 mL/min/1.73 m²
STAGE II CRF	GFR 60 - 89 mL/min/1.73 m²
STAGE III CRF	GFR 30 - 59 mL/min/1.73 m²
STAGE IV CRF	GFR 15 - 29 mL/min/1.73 m²
STAGE V CRF	GFR < 15 mL/min/1.73 m²

3.5/ HEART TRANSPLANTATION

INDICATION

Late-stage heart disease after optimal medical / surgical therapy, in presence of an unacceptable quality of life and a poor anticipated survival

Late-stage heart failure; Severe refractory ischemic symptoms; Refractory life-threatening arrhythmias; Complex congenital heart disease...

- **Cardiopulmonary stress testing** to guide transplant listing (reach anaerobic threshold)
 - Peak $\dot{V}O_2 \leq 12$ mL/kg/min (in the presence of a beta-blocker)
 - Peak $\dot{V}O_2 \leq 14$ mL/kg/min (patients intolerant to beta-blockers)
 - Percent of predicted peak $\dot{V}O_2 \leq 50\%$ (in young patients)
- **Heart failure prognosis score** to guide transplant listing
 - Seattle Heart Failure Model: 1-year survival $< 80\%$
 - Heart Failure Survival Score: High / Medium risk

ASSESSMENT

POTENTIAL DONOR: cold ischemia time < 4 h; TTE; coronary angiography (depending on risk factors / age); donor size

IMMUNOLOGICAL WORK-UP: blood group; antibody screening; Panel reactive antibody (PRA); specific HLA antibodies (directed against human leukocyte antigens)

➤ **PRA > 10 %:** recipient patient sensitized; ➤ risk of humoral rejection

• **Management:** IV Ig; Rituximab; plasmapheresis

CONTRAINDICATIONS

➤ **Fixed high pulmonary vascular resistances**

• Pulmonary vascular resistances > 5 WU

• Transpulmonary gradient (mPAP – Wedge) > 16-20 mmHg

• Pulmonary vascular resistance index (TPG / CI) > 6

• Pulmonary vascular resistances > 2.5 WU in response to pharmacological challenge while maintaining SBP > 85 mmHg (NO; Nitroprusside; Prostanoids; Inotropes)

• High risk of RV failure and mortality after cardiac transplantation

• Consider aggressive medical therapy (diuretics; inotropes; IV vasodilators; NO) and temporary mechanical support (IABP; LVAD) to improve these parameters

➤ **Others: A)** Irreversible renal dysfunction (GFR < 30 mL/min); **B)** Irreversible significant liver disease (biopsy PRN); **C)** Pre-existing cancer when the risk of tumor recurrence is significant; **D)** Active infection; **E)** Clinically severe symptomatic cerebrovascular disease; **F)** Peripheral arterial disease when it limits rehabilitation; **G)** DM with target organ damage or persistent poor glycemic control (HbA1c > 7.5%); **H)** Active mental illness / Nonadherence; **I)** Active smoking (previous 6 months) or active substance abusers (including alcohol); **J)** Obesity (BMI > 35 kg/m²); **K)** Age > 70 years old (consider selected patients); **L)** Frailty

PRIORITY ALLOCATION SYSTEM

STATUS 4	<ul style="list-style-type: none"> Dependent on mechanical support (or mechanical ventilation) and in the intensive care unit
STATUS 3.5	<ul style="list-style-type: none"> In-hospital inotrope-dependent (high doses or multiple agents) Highly sensitized patient Refractory life-threatening arrhythmia
STATUS 3	<ul style="list-style-type: none"> Uncomplicated LVAD / without intensive care In-hospital on inotropes (low dose / only one agent) Congenital heart disease <ul style="list-style-type: none"> ➤ arterial shunt-dependent ➤ with SaO₂ < 65 % ➤ complex with progressive arrhythmia ➤ complex with systemic ventricle decline Heart-lung transplantation
STATUS 2	<ul style="list-style-type: none"> In-patient Outpatient on inotropes Congenital heart disease <ul style="list-style-type: none"> ➤ with SaO₂ 65-75 % ➤ with Fontan and exudative enteropathy Multiple organ transplantation (other than heart-lung)
STATUS 1	<ul style="list-style-type: none"> Other

IMMUNOSUPPRESSION

INDUCTION

- **Anti-IL2 receptor antibodies** (Basiliximab) or **rATG** (antithymocyte immunoglobulins)
- **Precise indications:** high risk of rejection; risk of renal toxicity with calcineurin inhibitors

CORTICOSTEROIDS

- Decrease lymphocyte activation (T cells and B cells)
- Tapering after 6 months
- **Adverse effects:** Cushing; HTN; dyslipidemia; weight gain; DM; ulcers; cataracts; avascular necrosis of the hip; osteoporosis; shingles

CALCINEURIN INHIBITORS: CYCLOSPORINE OR TACROLIMUS

- Decrease T cell activation
- **Adverse effects:** Nephrotoxicity; HTN; DM; Neurotoxicity...



PURINE SYNTHESIS INHIBITORS: AZATHIOPRINE OR MMF (MYCOPHENOLATE MOFETIL)

- Inhibit T cell and B cell proliferation
- **Adverse effects:** Bone marrow suppression; Granulocytopenia; Diarrhea; Interaction with Allopurinol (Azathioprine)

M-TOR INHIBITORS: SIROLIMUS (RAPAMYCIN) AND EVEROLIMUS

- **Alternative to calcineurin inhibitors in the presence of renal toxicity**
- Block T cell (and B cell) activation
- Inhibit endothelial cell and fibroblast proliferation
 - > **Decrease the risk of cardiac allograft vasculopathy**
- **Adverse effects:** Altered healing

COMPLICATIONS

TRANSPLANT: bicaval anastomosis

POST-TRANSPLANT HEART FAILURE: optimize coronary perfusion; optimize RV preload (diuretics; UF; minimize transfusions); atrial pacing (junctional rhythm is common post-transplant); avoid hypercapnia - acidosis; inotropes (Milrinone; Dobutamine); pulmonary vasodilators (NO; Prostacyclins; Sildenafil); IABP - ECMO - RVAD - Impella

CELLULAR REJECTION: Lymphocyte infiltrates (T cells); several weeks to several years post-transplant; 40% in the first year

- > **Presentation:** ranges from asymptomatic to cardiogenic shock
- > **Diagnosis:** weekly biopsy for 6 weeks - monthly for 6 months - every 3 months for 2 years - every 4 to 6 months
- > **Risk factors:** Young age; female; CMV+; HLA incompatibility
- > **Treatment:** corticosteroids; intensification of immunosuppression

GRADE 0 R	Absence of rejection
GRADE 1 R (MILD)	Interstitial / Perivascular lymphocyte infiltration (≤ 1 zone of myocyte injury)
GRADE 2 R (MODERATE)	≥ 2 zones of infiltration with myocyte injury
GRADE 3 R (SEVERE)	Diffuse infiltration; multiple zones of myocyte injury (\pm edema; \pm bleeding; \pm vasculitis)

HUMORAL REJECTION (ANTIBODIES): anti-donor HLA antibody or anti-endothelial antigen antibody; absence of lymphocyte infiltrate; acute graft dysfunction (↘ LVEF)

➤ **Treatment:** Plasmapheresis; Corticosteroids; Rituximab

CLINICAL	<ul style="list-style-type: none"> Graft dysfunction; ↘ LVEF; Wall thickening (edema)
HISTOLOGICAL (BIOPSY)	<ul style="list-style-type: none"> Capillary endothelial congestion (± interstitial edema) Macrophages in capillaries (± neutrophils)
IMMUNO-PATHOLOGICAL	<ul style="list-style-type: none"> Immunofluorescence: Immunoglobulins + complement (C3d / C4d / C1q) in capillaries Immunohistochemistry: CD68+ macrophages in capillaries or C4d in capillaries
SEROLOGICAL	<ul style="list-style-type: none"> Anti-HLA class I or II antibodies or other anti-donor antibodies

CHRONIC REJECTION: chronic humoral rejection ± cardiac allograft vasculopathy

CARDIAC ALLOGRAFT VASCULOPATHY: 50% at 10 years; **diffuse concentric neointimal proliferation; no angina (denervation)**

- **Complications:** MI; allograft heart failure; arrhythmia; sudden death
- **Risk factors:** number of episodes of rejection; HLA incompatibility; conventional risk factors for CAD; graft ischemia time; donor age; CMV+...
- **Screening:** Dobutamine echocardiography; MIBI-P; Coronary angiography / IVUS
- **Treatment:** Statins; Control of conventional risk factors; Intensification of immunosuppression; m-TOR inhibitors; PCI; re-transplantation

INFECTION: nosocomial (early); fungal (Aspergillosis; Candidiasis); CMV (fever; leukopenia; transaminase elevation); HSV; VZV; PCP; Toxoplasmosis; TB; Nocardiosis; Cryptococcosis; *L. monocytogenes*

- **Prophylaxis (6-12 months post-transplant):** CMV (Acyclovir / Valganciclovir); *Pneumocystis carinii* and Toxoplasmosis (TMP/SMX); Antifungal agents (Voriconazole / Itraconazole)

NEOPLASIA: 30% at 10 years (lymphoma; cutaneous; solid organs)

OTHER COMPLICATIONS: HTN; Dyslipidemia; DM; CRF (calcineurin inhibitors); sinus tachycardia at rest (parasympathetic denervation); gout

- **Mean survival:** 10 years

3.6/ LONG-TERM VENTRICULAR ASSIST DEVICE

INDICATIONS

ADVANCED HEART FAILURE* <ul style="list-style-type: none"> NYHA IIb – IV and ≥ 2 of these elements: 	<ul style="list-style-type: none"> LVEF < 25% and/or VO₂ max < 14 mL/kg/min (or < 50% predicted for age / gender / BSA) Inotrope dependence Progressive target organ dysfunction due to hypoperfusion Repeated hospitalizations (≥ 3 per year) Progressive discontinuation of beneficial medication (ACE inhibitors; BB) due to hypotension or ARF
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*Estimated one-year mortality > 50% on medical therapy (Seattle Heart Failure Model; Heart Failure Survival Score)

SCENARIOS

BRIDGE TO DECISION	Acute hemodynamic collapse; maintain the patient alive in order to evaluate other therapeutic options; short-term / medium-term mechanical support (percutaneous or paracorporeal)
BRIDGE TO RECOVERY	Maintain the patient alive until recovery of sufficient cardiac function to wean mechanical support (by reverse remodeling); acute fulminant myocarditis or sometimes DCM or peripartum cardiomyopathy or following cardiac surgery or myocardial stunning
BRIDGE TO TRANSPLANTATION	Maintain the patient alive while waiting for transplantation
BRIDGE TO CANDIDACY	Improve target organ function to potentially make the patient eligible for transplantation
DESTINATION THERAPY	Use of long-term mechanical support (patient not a candidate for transplantation, but satisfactory life expectancy)

INTERMACS CLASSIFICATION

INTERMACS PROFILE		TIME TO MECHANICAL SUPPORT
1	CRASHING AND BURNING - Critical cardiogenic shock	Hours
2	PROGRESSIVE DECLINE - Positive inotrope-dependent; continuous deterioration	Days
3	STABLE BUT INOTROPE-DEPENDENT - Stable	Weeks
4	RECURRENT HEART FAILURE - Recurrent decompensation	Weeks - Months
5	EXERTION INTOLERANT - Comfortable at rest	Variable
6	EXERTION LIMITED - Fatigue with the slightest exertion	Variable
7	ADVANCED NYHA III - Comfortable at an acceptable level of exertion	Not a candidate

ASSESSMENT

Refer the patient for assessment before significant irreversible target organ damage (RV dysfunction; Irreversible PHT; irreversible congestive liver disease; irreversible renal failure; coagulopathy; malnutrition) +

- > **Target CVP < 15 mmHg** (decreases hepatic congestion; decreases the risk of post-LVAD right heart failure)

- > **Right ventricular stroke work index (RVSWI)** = $[(\text{mPAP} - \text{CVP}) \times \text{stroke volume}] / \text{BSA}$

- **Target RVSWI > 300 mmHg x mL/m²**

- **Mean PAP < 25 mmHg associated with low right ventricular reserve** +

- > **Liver disease:** risk of bleeding and post-op transfusion (with deterioration of RV function due to secondary volume overload)

- > **Assessments:** Target → BUN < 40 U/dL; creatinine < 221 μmol/L; GFR > 50 mL/kg/min; INR < 1.2; Hb > 100 g/L; Platelets > 150,000/mm³; Albumin > 30 g/L; Prealbumin > 15 g/L; ALT - AST < 2 ULN
- > **Valvular heart disease:** correct AR ≥ 3/4 or moderate MS or TR ≥ 3/4 or mechanical AVR

RISK OF POST-LVAD IN-HOSPITAL MORTALITY

PARAMETERS	POINTS	
Platelets < 148 000 / mm ³	7	POST-LVAD IN-HOSPITAL SURVIVAL <ul style="list-style-type: none"> • 0-8 points: 87.5 % • 9-16 points: 70.5 % • 17-19 points: 26 % • > 19 point: 13.7 % If ≥ 17 points: patient optimization prior to LVAD
Albumin < 33 g/L	5	
INR > 1.1	4	
Ongoing vasodilator therapy	4	
Mean PAP < 25 mmHg	3	
AST > 45 IU/mL	2	
Hematocrit < 34 %	2	
BUN > 51 U/dL	2	
Absence of IV inotrope	2	

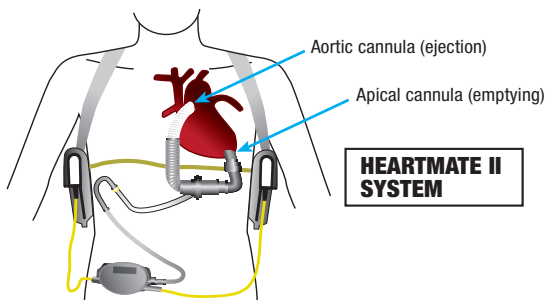
Lietz K, Long JW, Kfoury AG, et al. *Circulation*. 2007;116:497-505

LEFT VENTRICULAR ASSIST DEVICE (LVAD)

- “DESTINATION THERAPY” STUDIES:** ★ REMATCH (HEARTMATE XVE) and ★ HEARTMATE II →
- ↳ Mortality compared to conventional medical therapy; Improvement in NYHA class and quality of life; Reverse remodeling
 - > **2-year survival (registries):** 65 %

SECOND-GENERATION LVAD PUMPS: non-pulsatile flow (continuous); HeartMate II; Jarvik 2000

- > **Flow rate:** up to 10 L/min
- > **Pump speed:** adjusted by TTE (LV and RV chambers; position of IV septum; Ao valve opening every 3 beats)
- > **Anticoagulation:** Target INR 2 to 3 ± ASA 80 qd
- > **BP monitoring (continuous flow pump):** use sphygmomanometer and Doppler (target mean BP < 80 mmHg)



COMPLICATIONS: bleeding (acquired vWF deficiency; AV malformation); HIT; right heart failure; thromboembolism; stroke; infection; mechanical breakdown; fused aortic valve leaflets (leads to AR or AS); allosensitization; hemolysis; device thrombosis

THIRD-GENERATION PUMPS: HeartWare HVAD (intrapercardial)

MICROPUMPS: CircuLite Synergy (partial support up to 3 L/min; subclavian approach)

3.7/ RIGHT HEART FAILURE

ETIOLOGIES

- › Right heart failure secondary to left heart failure (most frequent)
- › Precapillary PHT (including pulmonary embolism)
- › Cardiomyopathy with RV involvement (including ARVD) (►► Chapter 5 - Cardiomyopathies)
- › RV infarction
- › Right valvular heart disease
- › Congenital heart disease (including ASD and intracardiac shunt)
- › Right heart failure post-cardiac surgery
- › Constrictive pericarditis (mimics right heart failure)

SYMPTOMS AND SIGNS

- › Fatigue; anasarca - edema; anorexia; nausea; RUQ pain
- › Hypotension; JVD ± Kussmaul; left parasternal heave; Harzer's sign; ± signs of PHT; right S3 (↗ inspiration); tricuspid regurgitation; hepatomegaly - pulsatile liver; systemic congestion (ascites; edema)

ASSESSMENT

TTE; radionuclide ventriculography; cardiac MRI; V/Q scintigraphy; Right-Left catheterization

MANAGEMENT

Diuretics (caution in the presence of normal Wedge pressure due to the risk of decreased LV preload); ± mineralocorticoid receptor antagonists

Specific treatment of PHT; Specific treatment of LV HF

Surgical or percutaneous correction of structural abnormality (valvular or congenital malformation)

3.8/ PALLIATIVE CARE

- › Discussing the patient's wishes at the stage of advanced heart failure
- › Good communication with the patient and family
- › Desactivation of the defibrillator
- › Analgesia
- › ± IV diuretics; ± palliative IV inotropes

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Valvular heart disease

04

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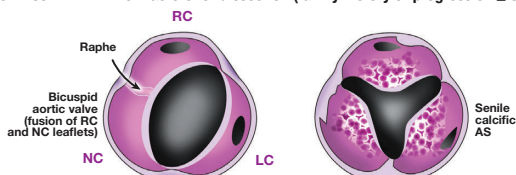
4.1/ AORTIC STENOSIS

ETIOLOGIES

SENILE CALCIFIC AS: Similar risk factors and pathophysiology to CAD and mitral annular calcification (MAC)

BICUSPID AORTIC VALVE

- > 1-2% of the population
- > **70-80%: fusion of right and left coronary leaflets**
 - 20-30%: fusion of right coronary and non-coronary leaflets
 - Fusion of non-coronary and left coronary leaflets is rare
- > **TTE:** Demonstrates valve opening during systole with **only two commissures** (unicuspid valve: only one commissure)
- > Screening TTE should be performed in 1st degree relatives
- > **Associated aortopathy** (medial degeneration); **aneurysm; dissection** +
 - Imaging (TTE; CT angiography; MRI) annually if aorta > 45 mm
 - BB if aorta > 40 mm (in the absence of significant AR)
 - **Ascending aorta replacement if aorta > 55 mm (> 45 mm when AVR is also necessary) or > 50 mm with risk factors for dissection (family history or progression \geq 5 mm/year)**



RHEUMATIC: fusion of commissures; triangular orifice; concomitant AR and AS; associated mitral valve disease in the majority of cases

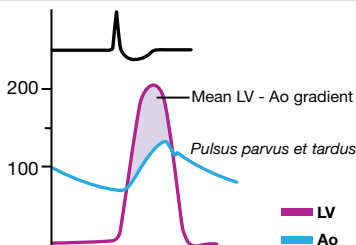
CONGENITAL AORTIC STENOSIS (can be treated by balloon valvuloplasty)

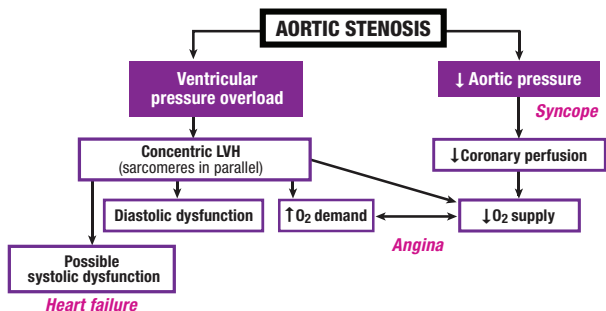
RHEUMATOID AORTIC STENOSIS (rare)

DDx: Aortic sclerosis (calcification but **peak velocity < 2.5 m/s**); HCM (dynamic obstruction)

- > **Supravalvular aortic stenosis: strong A2;** murmur radiates to the right carotid; BP right arm > BP left arm; associated with Williams syndrome
- > **Subvalvular aortic stenosis:** membrane or tunnel; combined with AR; absence of systolic anterior motion (SAM) of mitral leaflet

HEMODYNAMIC CONSEQUENCES





SYSTOLIC DYSFUNCTION SECONDARY TO:

- 1) **↘ Intrinsic contractility** secondary to remodeling (only slight improvement with surgery)
- 2) **Mismatch between high afterload and insufficient concentric LVH** (afterload mismatch) (improved by surgery)

SEVERITY

NORMAL AREA: 3-4 cm²

	MILD	MODERATE	SEVERE	CRITICAL
Jet velocity (m/s)	2.6-2.9	3.0 - 4.0	> 4.0	> 5.0
Mean gradient (mmHg)	< 20	20 - 40	> 40	> 60
Valve area (cm ²)	> 1.5	1.0 - 1.5	< 1.0	< 0.6
Indexed valve area (cm ² /m ²)	> 0.85	0.6 - 0.85	< 0.6	
LVOT VTI / Ao valve VTI ratio	> 0.50	0.25 - 0.50	< 0.25	

SYMPTOMS AND SIGNS

SYMPTOMS: Heart failure / Dyspnea; Angina; Syncope

- Bleeding (destruction of von Willebrand factor; Heyde's syndrome)

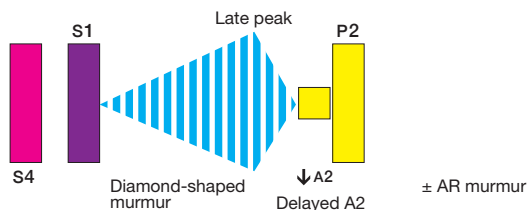
CAROTID: *pulsus parvus et tardus* (slow ascent; late peak; low amplitude) (absent in the presence of arteriosclerosis); carotid thrill

APEX: sustained; lateralized if LV dysfunction; S4 sometimes palpable; **apical-carotid delay**

AORTIC AREA: look for **thrill**

AUSCULTATION: **crescendo - decrescendo murmur with late peak**; carotid radiation; radiation to apex in the case of Gallavardin phenomenon (high-pitched murmur); accentuation of murmur post-PVC; decrescendo diastolic murmur in the presence of associated AR

- **S2 with a single component:** **Inaudible A2** or delayed A2 and at same time as P2 with paradoxical expiratory splitting
- **S4**
- **Systolic ejection click** of bicuspid aortic valve disappears in the case of ↘ valve mobility



INVESTIGATIONS

STRESS TEST: To distinguish asymptomatic from symptomatic aortic stenosis; contraindicated if the patient presents symptoms of AS

- > Look for symptoms - decreased exercise capacity (< 80% predicted) - abnormal BP response (\nearrow SBP < 20 mmHg)

ECHOCARDIOGRAPHIC FOLLOW-UP

MILD AS	MODERATE AS	SEVERE ASYMPTOMATIC AS
TTE every 3 to 5 years	TTE every 1 to 2 years	TTE every 6 months to 1 year

HEMODYNAMIC ASSESSMENT - INDICATIONS

- Inconclusive noninvasive investigation
- Discordance between clinical findings and noninvasive investigation

PREOPERATIVE CORONARY ANGIOGRAPHY - INDICATIONS

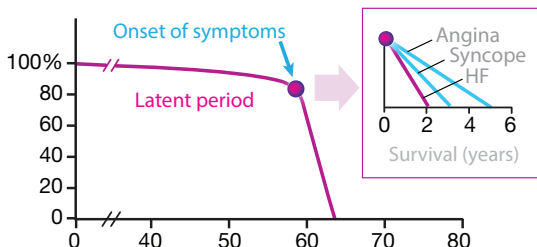
- > Angina; documented ischemia; LV systolic dysfunction; known CAD; Male > 40 years; postmenopause; cardiovascular risk factors
- Consider coronary CT angiography in patients with low-to-moderate pretest probability of CAD
- It is reasonable not to perform preoperative coronary angiography in a surgical emergency in the presence of acute valvular regurgitation, acute aortic syndrome or bacterial endocarditis (class IIa recommendation)

OUTCOME

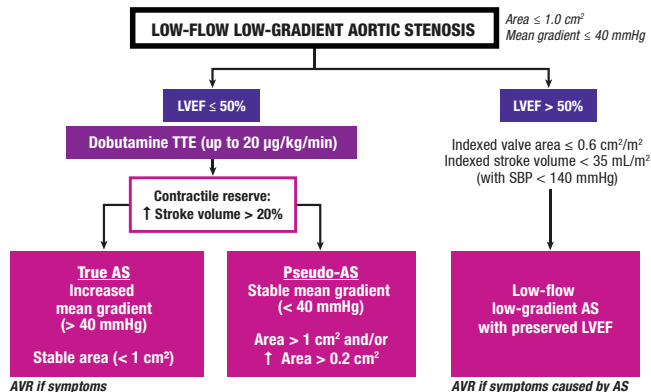
\searrow Valve area by 0.1 cm^2 / year; \nearrow Mean gradient by 7 mmHg / year

Asymptomatic AS: risk of sudden death < 1% / year

Symptomatic AS: \searrow survival (sudden death); 2 years in the presence of HF; 3 years in the presence of syncope; 5 years in the presence of angina



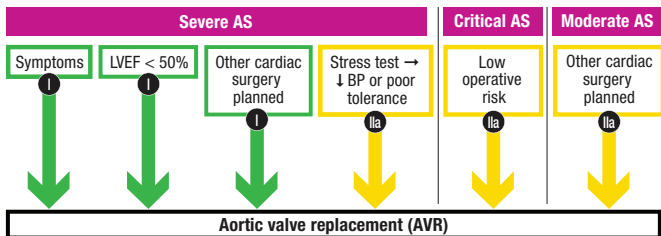
LOW-FLOW LOW-GRADIENT AORTIC STENOSIS



MANAGEMENT

MEDICAL: Patient education - report all symptoms; avoid strenuous physical exertion; echocardiographic follow-up; low-dose diuretics; avoid BB; cautious use of vasodilators (fixed obstruction); treatment of cardiovascular risk factors

SURGERY - INDICATIONS



> **Complication of AVR:** mortality 1-3%; stroke 2%; prolonged ventilation 11%; thromboembolism; bleeding; prosthetic dysfunction

PERCUTANEOUS BALLOON VALVULOPLASTY

Risk of major complications > 10%

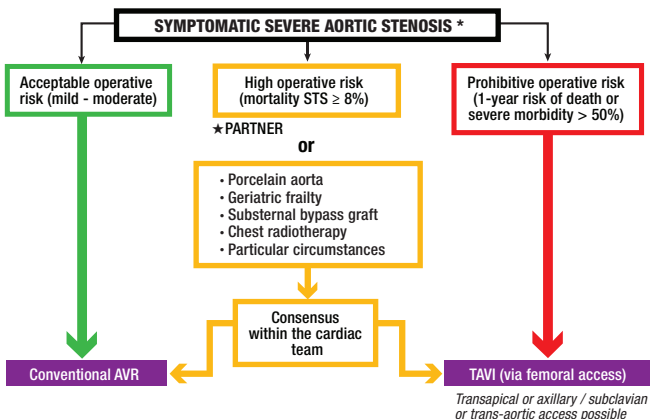
Recurrent symptoms and restenosis at 6 months

Does not constitute a medium-term or long-term alternative to AVR or TAVI

LIMITED INDICATIONS: bridge to AVR or TAVI in a patient with severe symptoms

> Effective in adolescents / young adults with congenital AS in the absence of calcification

TAVI (Transcatheter aortic valve implantation)



* Absence of futility: an operation will probably improve life span and/or quality of life; survival with treatment will probably be $\geq 1-2$ years

PRE-TAVI ASSESSMENT: **A)** TTE; **B)** TEE: aortic annulus dimensions at insertion of leaflets on anteroposterior view (PLAX) and side-to-side (short-axis); **C)** CT angiography: Ao; aortic annulus dimensions; aortic-iliac-femoral PAD; distance between coronary ostia and aortic annulus; **D)** Coronary angiography - Aortography - Ventriculography

- > Aortic annulus diameter: **> 18 mm and < 29 mm**
- > Coronary ostia - aortic annulus distance **$\geq 10-11$ mm**
- > Femoral vascular access: **femoral artery diameter > 6 mm** (to accommodate a 7 mm catheter); evaluate the degree of calcification and arterial tortuosities
- > **Geriatric frailty:** increased risk of adverse events during major surgery; **5-meter walking time > 6 s**; Katz index of independence in ADL

STEPS OF THE FEMORAL APPROACH: **A)** Femoral access; **B)** Transvalvular guide; **C)** Delivery catheter; **D)** Pre-dilatation by valvuloplasty during rapid ventricular pacing (180-200 bpm); **E)** Positioning of the valve under fluoroscopic / angiographic guidance and/or by TEE (50% above and 50% below the plane of the aortic annulus); **F)** Valve deployment during rapid ventricular pacing (180-200 bpm) (Sapien valve); **G)** Identification and management of complications; **H)** Closure of access site

LIMITED BENEFIT OF TAVI: Life expectancy < 1 year; 2-year survival with estimated benefit < 25%; STS > 15% (no benefit on survival in ★ PARTNER B); advanced geriatric frailty (dependence for multiple ADL); multiple comorbidities

COMPLICATIONS: 30-day mortality: 3-5%; stroke (6-7%); vascular complications (17%); valve embolization; coronary occlusion (due to migration of a leaflet or calcification); mitral valve disease; perivalvular regurgitation (incomplete apposition); tamponade; AV block requiring PPM (2-9% Sapien; 19-43% Corevalve); arrhythmias; bleeding; aortic rupture

POST-TAVI MANAGEMENT: Long-term ASA; Thienopyridine for 1 to 6 months (except when treated with warfarin); prophylactic antibiotics; annual clinical and TTE follow-up

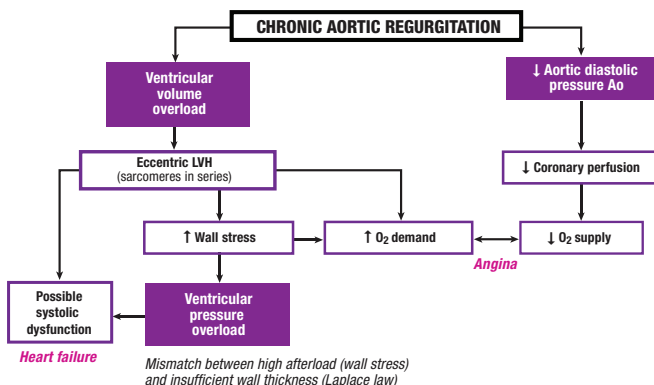
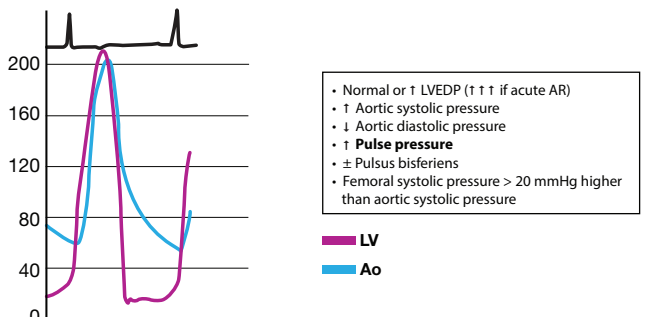
4.2/ CHRONIC AORTIC REGURGITATION

ETIOLOGIES

VALVULAR: **A)** Degenerative (calcification); **B)** Endocarditis; **C)** Leaflet prolapse (loss of support due to aortopathy); **D)** Bicuspid aortic valve; **E)** Rheumatic; **F)** VSD; **G)** Subaortic membrane; **H)** Iatrogenic (post-balloon valvuloplasty); **I)** Myxomatous proliferation; **J)** SLE - RA - ankylosing spondylitis

AORTIC: **A)** Aortic dilatation: degenerative / cystic medial necrosis (isolated; Marfan; bicuspid aortic valve); osteogenesis imperfecta; syphilis; Behçet; Takayasu; giant cell arteritis; spondyloarthropathies / ankylosing spondylitis / psoriatic arthritis; polychondritis; HTN; **B)** Dissection: leaflet prolapse following loss of support or presence of intravalvular flap or leaflet perforation by dissection; **C)** Traumatic

HEMODYNAMIC CONSEQUENCES



SEVERITY

	MILD AR (1/4)	MODERATE AR (2 to 3/4)	SEVERE AR (4/4)
Vena contracta (mm)	< 3	3 - 5.9	≥ 6
Regurgitant volume (mL/b)	< 30	2/4: 30 - 44 3/4: 45 - 59	≥ 60
Regurgitant fraction (%)	< 30	30 - 49	≥ 50
Regurgitant orifice (cm ²)	< 0.10	2/4: 0.1 - 0.19 3/4: 0.2 - 0.29	≥ 0.30
Jet width (PLAX)	Central; < 25% of LVOT	Intermediate	> 65% of LVOT
Area of regurgitant jet (PSAX)	< 5 % of LVOT area	Intermediate	> 60 % of LVOT area
Pressure half-time (ms)	> 500	200-500	< 200
Diastolic reversal of descending Ao	Brief; Early diastolic	Intermediate	Holodiastolic and prominent (end- diastolic velocity > 20 cm/s)
LV dimensions	Normal		Dilatation
Angiography	1+	2+	3-4+

OTHER MARKERS OF SEVERITY: Holodiastolic reversal of flow in proximal abdominal aorta

SYMPTOMS AND SIGNS

SYMPTOMS: Heart failure - Dyspnea; Angina; Tiredness

- > Poorly tolerated bradycardia (↗ regurgitation time)

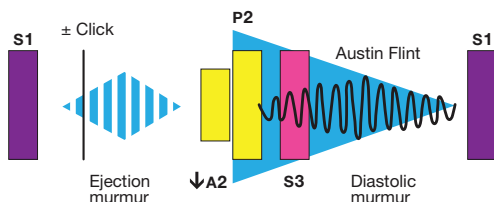
VITAL SIGNS: ↗ pulse pressure (with ↘ DBP)

PULSE: bounding; *pulsus bisferiens* (more accurately assessed in brachial or femoral arteries); carotid thrill (↗ stroke volume)

APEX: large; hyperdynamic; lateralized; ± palpable S3

AUSCULTATION: **decrescendo diastolic murmur starting at A2;** more accurately assessed with the patient seated and leaning forward in forced expiration; duration correlated with severity

- > Murmur increases with fists clenched
- > **Radiation to left parasternal region indicates a valvular etiology; Radiation to right parasternal region indicates an aortic etiology**
- > **Decreased A2** indicates a valvular etiology
- > Systolic ejection click (abrupt distension of the aorta)
- > **S3**
- > **Systolic ejection murmur** (↗ stroke volume) ± thrill
- > **Austin Flint murmur:** diastolic rumbling due to aortic reflux onto anterior mitral leaflet
- > **Distinguish AR from PR:** AR → murmur starting at A2; peripheral signs; PR murmur ↗ during inspiration

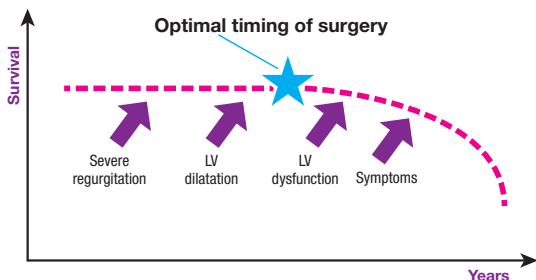


Musset's sign	Systolic nodding of the head
Müller's sign	Systolic pulsation of uvula
Quincke's sign	Capillary pulsation (by pressing lightly on the tip of the nail)
Corrigan's pulse / Water hammer pulse	Abrupt distension with prominent pulse then rapid collapse (more accurately assessed in the radial artery with the arms raised)
Traube's sign (pistol shot)	Systolic and diastolic bruit in the femoral artery
Duroziez' sign	Systolic murmur in the femoral artery with proximal compression and diastolic murmur with distal compression (from the stethoscope)
Hill's sign	SBP in arms > 20 mmHg higher than SBP in legs

OUTCOME AND FOLLOW-UP

Survival rate declines markedly in the presence of symptoms or LV dysfunction

> **Mortality in the presence of symptoms:** > 10 % / year

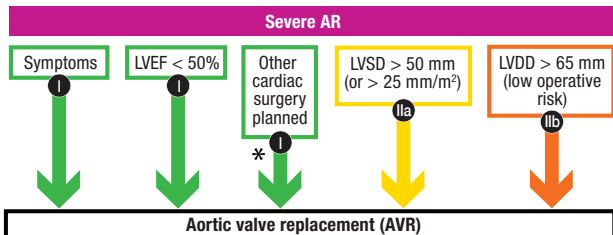


NEWLY DIAGNOSED AR	MILD AR	MODERATE AR	SEVERE AR	SEVERE AR WITH LV DILATATION
TTE at 3 months to ensure stability	TTE every 3 to 5 years	TTE every 1 to 2 years	TTE every 6 to 12 months	TTE every 4 to 6 months

MANAGEMENT

MEDICAL: patient education - report all symptoms; avoid strenuous physical exertion / isometric exercises; echocardiographic follow-up; treat diastolic HTN (ACE inhibitors or Nifedipine); avoid bradycardia; ACE inhibitors and beta-blockers if poor candidate for surgery with severe AR with symptoms and/or LV dysfunction

SURGERY: AVR vs AVR + ascending aorta replacement (Bentall) vs Valve repair vs Ascending aorta replacement + valvular resuspension (David procedure) vs Ross procedure



* IIa if moderate AR

4.3/ ACUTE AORTIC REGURGITATION

ETIOLOGIES: **A)** Endocarditis; **B)** Aortic dissection; **C)** Trauma; **D)** Prosthetic valve dysfunction

HEMODYNAMIC CONSEQUENCES: Regurgitant volume in poorly compliant LV → ↑↑ diastolic pressures → Congestive heart failure

- ↘ Anterograde flow → Systemic hypoperfusion / Shock
- Early mitral valve closure (restrictive diastolic filling pattern)

PHYSICAL EXAMINATION: Tachycardia; shock; pulmonary edema

- ↘ S1 (early mitral valve closure); S3 and S4
- **Brief diastolic murmur** (early pressure equalization on either side of the valve)
- **Austin Flint rumble**
- Systolic murmur (↗ stroke volume)
- Signs of PHT

MANAGEMENT: Urgent surgery

- Positive inotropic agent (Dobutamine) and/or vasodilator (Nitroprusside)

4.4/ MITRAL STENOSIS

ETIOLOGY

RHEUMATIC FEVER: Leading cause of MS

- 25% of patients have isolated MS; 40% have MS and MR; 35% have concomitant aortic valve disease; 6% have concomitant tricuspid valve disease

OTHER RARE CAUSES: **A)** Congenital; **B)** Carcinoid with lung metastases or PFO; **C)** SLE; **D)** RA; **E)** Hunter-Hurler; **F)** Fabry; **G)** Whipple; **H)** Methysergide; **I)** Calcific MS (age related)

DDX (LV INFLOW OBSTRUCTION): LA tumor - Myxoma; LA thrombus; Obstructive vegetation; Cor triatriatum; Severe mitral annular calcification (age); Pulmonary vein stenosis

SEVERITY

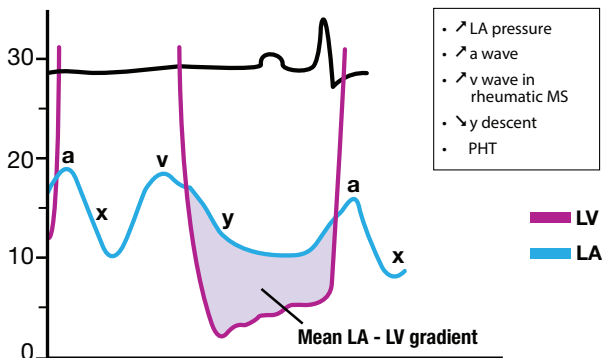
NORMAL AREA: 4-5 cm²

	MILD	MODERATE	SEVERE
Valve area (cm ²)	> 1.5	1.0 - 1.5	< 1.0
Mean gradient (mmHg)	< 5	5 - 10	> 10
sPAP (mmHg)	< 30	30 - 50	> 50
Pressure half-time (ms)		150 - 220	> 220 ms

Indices valid for heart rate between 60 and 90 bpm

HEMODYNAMIC CONSEQUENCES

- LA pressure → pulmonary congestion / PHT / Right heart failure
- LA dilatation → risk of AF / atrial stasis / peripheral embolism
- Intolerance of tachycardia or loss of atrial kick
- Low output state



SYMPTOMS AND SIGNS

SYMPTOMS: Dyspnea; tiredness; poor exercise tolerance; OTP; PND

- **PHT:** Right heart failure; hemoptysis (rupture of bronchial veins; rupture of capillaries; pulmonary edema)
- Palpitations; peripheral embolism
- Recurrent laryngeal nerve compression by dilated LA (Ortner's syndrome)

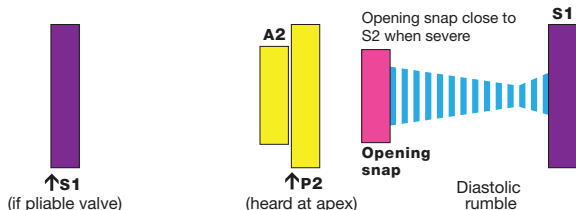
MITRAL FACIES: secondary to systemic vasoconstriction; pink-purple plaques on cheeks**JUGULAR:** JVD; prominent a wave (sinus rhythm)**AUSCULTATION:** S1 when leaflets still pliable and only slightly calcified

OPENING SNAP: Heard more clearly with the diaphragm; absent during significant leaflet calcification

- > **A2 - opening snap interval inversely proportional to the severity of MS (severe if < 80 ms)**

DIASTOLIC RUMBLE: Heard more clearly in left lateral supine position with the bell at the apex; look for thrill; murmur increased during tachycardia - exercise

SIGNS OF PHT: left parasternal heave; **P2 increased** (\pm palpable); ejection click (PA dilatation); TR murmur; Graham Steell murmur; right S3-S4



INVESTIGATIONS AND OUTCOME

TTE: Rheumatic MS \rightarrow thickening \pm calcification of leaflets; hockey stick appearance of anterior mitral leaflet; LA dilatation; commissural fusion with “fish-mouth” mitral orifice (PSAX)

ECHOCARDIOGRAPHIC FOLLOW-UP

MILD MS	MODERATE MS	SEVERE MS
TTE every 3 to 5 years	TTE every 1 to 2 years	TTE annually

STRESS TEST: Evaluate exercise capacity and symptoms

- > Combined with TTE to evaluate PAP and mean gradient on exertion when there is a discordance between symptoms and TTE at rest

OUTCOME: Valve area \searrow by $0.09 \text{ cm}^2/\text{year}$

- > 5-year survival in patients with symptomatic severe MS without intervention: 44%

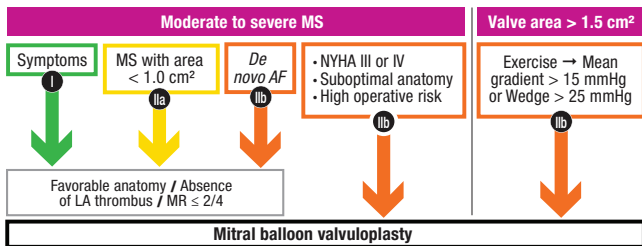
MANAGEMENT

MEDICAL: prevention of recurrence of rheumatic fever (penicillin-based prophylactic antibiotics); avoid strenuous exertion; follow-up and decision to operate at the optimal time; aggressive treatment of AF and thromboembolic risk; diuretics PRN; avoid tachycardia

- > **Indication for anticoagulation:** AF; Cardioembolic history; LA thrombus

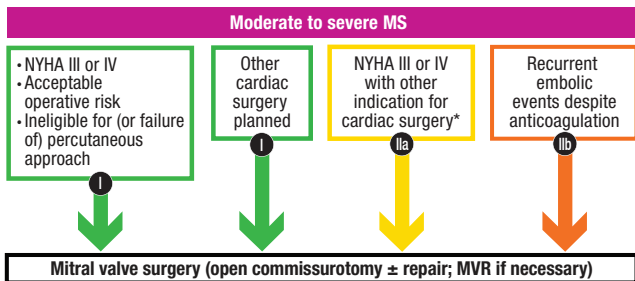
BALLOON MITRAL VALVULOPLASTY: transseptal approach; TEE guidance; Inoue 23 to 25 mm balloon; inflation of the balloon inside the valve orifice in order to open commissures

- > **Better results in a context of favorable anatomy: Wilkins score (BVR) ≤ 8 points** +
 - **Success:** valve area $> 1.5 \text{ cm}^2$ and LA pressure $< 18 \text{ mmHg}$
- > **Contraindications:** moderate to severe MR; LA thrombus (pre-procedure TEE); unfavorable anatomy
- > **Complications:** mortality 1%; stroke - embolism 1-2%; cardiac perforation 1%; MR requiring surgery 2%; iatrogenic ASD; myocardial infarction $< 1\%$



SURGICAL APPROACH: **A)** Closed commissurotomy (obsolete approach); **B)** Open commissurotomy ± mitral valve repair (under CPB); **C)** MVR

- Consider MAZE and LAA amputation during surgery (★ CTSN AF)



* TR; CAD; aortic valve disease; aortic aneurysm, etc.

4.5/ CHRONIC MITRAL REGURGITATION

ETIOLOGY

DEGENERATIVE: **MVP - Myxomatous disease;** Marfan; Ehlers-Danlos; Pseudoxanthoma elasticum; Mitral annular calcification

INFLAMMATORY: **Rheumatic disease;** SLE; Scleroderma; Hypereosinophilia syndrome

INFECTIOUS: Endocarditis

STRUCTURAL: **Ruptured chordae tendineae** (spontaneous - idiopathic; MI; trauma; MVP; endocarditis; rheumatic fever; acute LV dilatation)

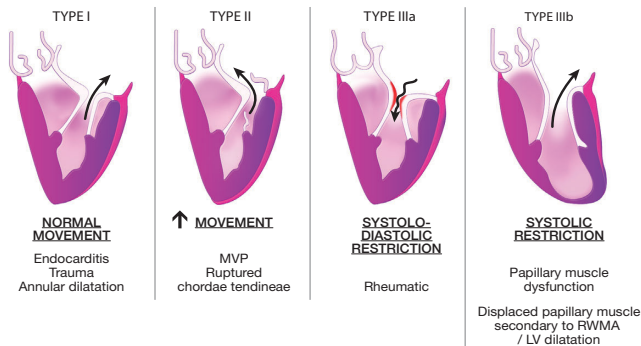
CONGENITAL: Cleft mitral valve; parachute mitral valve (absence of mitral papillary muscle)

FUNCTIONAL MR: associated with LV dysfunction / LV dilatation; **structurally normal valve;** MR secondary to: **A)** Mitral papillary muscle displacement (malcoaptation of leaflets; tenting area > 6 cm² associated with MR ≥ 3/4; **B)** Annular dilatation; **C)** Loss of the annular systolic contraction; **D)** ± Mitral papillary muscle dysfunction in the presence of concomitant ischemia

- **Ischemic papillary muscle dysfunction: posteromedial muscle (perfusion by PDA)**
 >> anterolateral muscle (double perfusion by diagonal and marginal arteries)

CARPENTIER'S CLASSIFICATION

According to movement of the leaflets

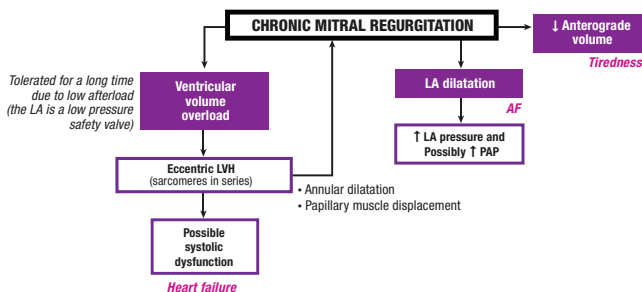
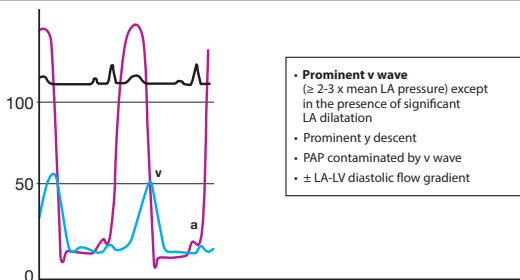


SEVERITY

	MILD MR (1/4)	MODERATE MR (2 to 3/4)	SEVERE MR (4/4)
Veina contracta (mm)	< 3	3 - 6.9	≥ 7
Regurgitant volume (mL/b)	< 30	2/4: 30 - 44 3/4: 45 - 59	≥ 60
Regurgitant fraction (%)	< 30	30 - 49	≥ 50
Regurgitant orifice (cm²) (prognostic value)	< 0.20	2/4: 0.2 - 0.29 3/4: 0.3 - 0.39	≥ 0.40
Jet area	Small central jet < 4 cm ² or < 20% of LA area	Intermediate	Large central jet > 10 cm ² (or > 40% of LA area) or eccentric jet along the LA wall (Coanda)
Pulmonary vein flow rate	Systolic dominance	Systolic attenuation	Systolic reversal
Jet envelope on continuous Doppler	Faint; parabolic	Intermediate	Dense; Early, triangular peak
LA dimensions	Normal		Dilatation
LV dimensions	Normal		Dilatation
Angiography	1+	2+	3-4+

FUNCTIONAL MR: severe regurgitation when regurgitant orifice ≥ 0.20 cm² or regurgitant volume ≥ 30 mL/b or regurgitant fraction $\geq 50\%$

HEMODYNAMIC CONSEQUENCES



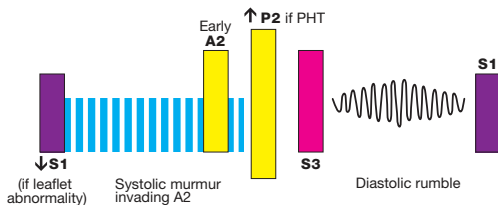
SYMPTOMS AND SIGNS

SYMPTOMS: Dyspnea; OTP; PND; symptoms of low output state; Palpitations (AF); Right heart failure

APEX: hyperdynamic; **dilated; lateralized;** \pm palpable S3; palpable wave in left parasternal region (dilated LA kick)

AUSCULTATION: **Decreased S1** in the presence of a leaflet abnormality; early A2 and split S2; $P2 > A2$ in the presence of PHT; S3; diastolic rumble (\nearrow inflow)

SYSTOLIC MURMUR: spreads as far as (and invades) A2; **often holosystolic;** \pm thrill; high-pitched; maximum at the apex; radiation to the axilla or left scapula (posteriorly directed murmur) or sternum and base (anteriorly directed murmur as in posterior leaflet MVP); not amplified post-PVC; decreased by standing up (increased by squatting); decreased during Valsalva; increased by clenching the fists (in contrast with aortic stenosis)



DDx: A) VSD: murmur maximal in left parasternal region; thrill in left parasternal region; **B)** TR: murmur \nearrow on inspiration; murmur maximal in left parasternal region; prominent jugular v wave

ISCHEMIC PAPILLARY MUSCLE DYSFUNCTION: mid-systolic or end-systolic murmur

ECHOCARDIOGRAPHIC FOLLOW-UP

MILD MR	MODERATE MR	SEVERE MR
TTE every 3 to 5 years	TTE every 1 to 2 years	TTE 6 to 12 months

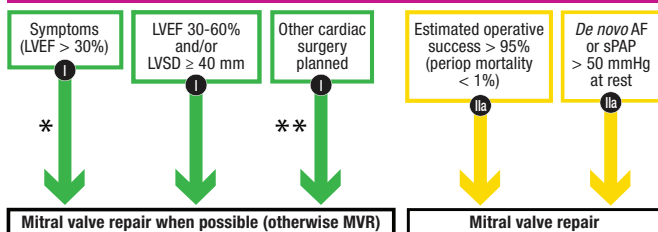
TTE to clarify the anatomy, mechanism, severity and possibility of repair

Stress echocardiography PRN to detect ischemic MR and to measure PAP on exertion

MANAGEMENT

MEDICAL: little benefit of vasoactive agents in the presence of normal LVEF (afterload is rarely increased except in HTN); anticoagulation in the presence of AF; aggressive treatment of LV dysfunction in the presence of functional MR (+ resynchronization)

Severe chronic primary MR



IIb: Consider Mitraclip when surgery is contraindicated in NYHA III or IV with favorable anatomy

*IIb: Symptoms and LVEF < 30%

** IIa: Moderate chronic primary MR (mitral valve repair)

MITRAL VALVE REPAIR / ANNULOPLASTY: Best candidates (in the absence of calcification)

→ **A)** Degenerative MR - MVP (posterior leaflet easier to repair); **B)** Annular dilatation; **C)** Papillary muscle dysfunction; **D)** Ruptured chordae tendineae; **E)** Leaflet perforation (endocarditis)

- > Possible via a minimally invasive approach
- > Warfarin for 3 months post-repair; ASA 80 indefinitely

MVR: opt for preservation of the subvalvular apparatus whenever possible (LVEF \searrow by 10% if loss of the subvalvular apparatus due to modification of LV geometry)

MITRALCLIP: percutaneous transseptal repair; creation of a double orifice valve using a clip (equivalent to Alfieri procedure)

- > ★ **EVEREST:** Mitraclip less effective than conventional surgery to reduce the degree of regurgitation
- > **Candidates:** inoperable patient; mitral regurgitation with **regurgitant jet due to malcoaptation of segments A2 and P2**; functional or degenerative regurgitation (MVP or leaflet eversion); depth of coaptation < 11 mm; vertical length of coaptation > 2 mm

FUNCTIONAL MR: ►► Chapter 3

MITRAL VALVE PROLAPSE

2.4% of the population; female predominance

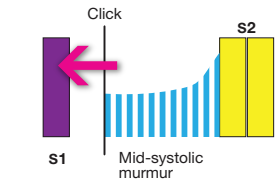
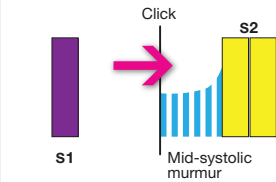
DIAGNOSIS: **A)** Mid-systolic click then murmur; **B)** Displacement of one or both leaflets > 2 mm behind the plane of the mitral annulus (**PLAX**); **C)** \pm Thickening of the leaflets by > 5 mm

ETIOLOGIES

- MVP syndrome:** young woman; benign; associated with OH - palpitations - anxiety; thin leaflets
- MVP with myxomatous thickening:** often males aged 40-70 years; thickening / redundancy of the leaflets; significant risk of progression; risk of ruptured chordae tendineae
- MVP associated with another disease:** Marfan; HCM; Ehlers-Danlos; osteogenesis imperfecta; *pseudoxanthoma elasticum*; Holt-Oram syndrome; *ostium secundum* ASD; Ebstein's anomaly

CLINICAL FEATURES: mid-systolic click then mid- or end-systolic murmur (often crescendo); normal S1; dynamic auscultation

- Mid-systolic click different from the aortic ejection click, as it occurs after the onset of the carotid upstroke

DECREASED LEFT INTRAVENTRICULAR VOLUME	INCREASED LEFT INTRAVENTRICULAR VOLUME
<p>Effect: \nearrow duration of MVP murmur</p>  <p>Click</p> <p>S1</p> <p>Mid-systolic murmur</p> <p>S2</p>	<p>Effect: \searrow duration of MVP murmur</p>  <p>Click</p> <p>S1</p> <p>Mid-systolic murmur</p> <p>S2</p>
<p>Maneuvers:</p> <ul style="list-style-type: none"> • Bradycardia • \searrow Afterload • \nearrow Contractility • \searrow Venous return (standing; Valsalva) 	<p>Maneuvers:</p> <ul style="list-style-type: none"> • Bradycardia • \nearrow Afterload (clenched fists) • \searrow Contractility • \nearrow Venous return (squatting; raising legs)

COMPLICATIONS: Heart failure; Ruptured chordae tendineae; Thromboembolism; Endocarditis; AF; serious complications (including surgery) in 1/100 patient-years

- TIA:** ASA 80 mg qd
- AF:** anticoagulation if > 65 years or HTN or MR or history of heart failure
- Stroke:** anticoagulation if MR or AF or LA thrombus or leaflets > 5 mm

4.6/ ACUTE MITRAL REGURGITATION

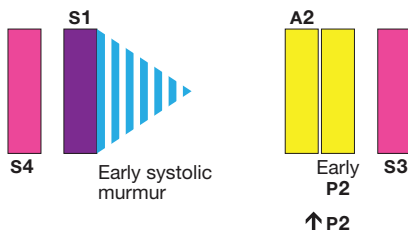
ETIOLOGIES: **A)** Endocarditis; **B)** Trauma - iatrogenic; **C)** Ruptured chordae tendineae (idiopathic-spontaneous; myxomatous degeneration / MVP; Marfan; Ehlers-Danlos; endocarditis; acute rheumatic fever; trauma); **D)** Papillary muscle dysfunction or rupture (ischemia - MI); **E)** Prosthetic valve dysfunction

HEMODYNAMIC CONSEQUENCES: Acute MR \rightarrow poorly compliant LA (significant v wave)

\rightarrow pulmonary congestion / PHT

- Acute MR \rightarrow low anterograde flow

PHYSICAL EXAMINATION: **Decrescendo early systolic murmur** due to rapid equalization of pressures on both sides of the valve; **S3 and S4**; signs of PHT; early closure of pulmonary valve (early P2); pulmonary overload; hypotension; tachycardia



MANAGEMENT: Urgent surgery in the presence of heart failure

- **Medical treatment:** Nitroprusside (\pm Dobutamine) while waiting for surgery; IABP

4.7/ TRICUSPID STENOSIS

ETIOLOGIES: **Rheumatic** (majority); usually associated with MS

- **Other causes (rare):** Congenital atresia; RA tumor; Carcinoid syndrome ($TR \gg TS$); PPM lead; Extracardiac tumor; Thrombus; Endomyocardial fibrosis; Endocarditis; SLE

SEVERITY: Significant TS when valve area $\leq 1 \text{ cm}^2$ or mean gradient $\geq 5 \text{ mmHg}$ or pressure halftime $> 190 \text{ ms}$

JUGULAR: Prominent a wave; Loss of y descent

AUSCULTATION: **diastolic rumble in lower left parasternal region with \nearrow on inspiration** (\pm thrill); murmur \nearrow on **Mueller maneuver** (inspiration against closed glottis) or during exercise

- Opening snap following that of MS in lower left parasternal region
- Diastolic rumble of the MS; Opening snap

SIGNS OF RIGHT HEART FAILURE (ascites; HSM; peripheral edema; JVD)

MANAGEMENT: operation if **severe symptomatic TS or severe TS with concomitant mitral surgery**

- Open commissurotomy vs TVR (bioprosthesis) vs Balloon valvuloplasty

4.8/ TRICUSPID REGURGITATION

ETIOLOGIES: **Secondary / Functional** (majority); secondary to dilatation of the tricuspid annulus following dilatation of the RV (sPAP $> 55 \text{ mmHg}$; RV infarction; PS; DCM; left heart failure...)

- **Primary causes:** Rheumatic; Endocarditis; Ebstein's anomaly; Prolapse (associated with MVP); Carcinoid; Papillary muscle dysfunction / Ruptured chordae tendineae; Trauma; Marfan; RA; Radiotherapy; AV canal defect; Endomyocardial fibrosis; Myxoma; PPM lead; Repeated biopsy (heart transplant); anorectics; SLE

SEVERITY

	MILD TR (1/4)	MODERATE TR (2 – 3/4)	SEVERE TR (4/4)
Jet area (central) cm ²	< 5	5 - 10	> 10
Vena contracta (mm)			≥ 7
PISA radius (mm)	≤ 5	6 - 9	> 9
Tricuspid E (m/sec)			> 1
Jet envelope on continuous Doppler	Faint; parabolic	Intermediate	Dense; Early, triangular peak
Hepatic vein flow	Systolic dominance	Systolic attenuation	Systolic reversal

- **Other criteria:** tricuspid annulus ≥ 40 mm (or > 21 mm/m²); D-shaped septal curvature; RV - RA dilatation; EROA ≥ 0.4 cm²; regurgitant volume ≥ 45 mL/b

INSPECTION: Cachexia; Jaundice; Pulsatile orbits

JUGULAR: Prominent c-v wave; loss of x descent; prominent y descent; ± venous thrill; Kussmaul

PALPATION: left parasternal heave; RV lift

AUSCULTATION: **Right S3** (↗ on inspiration); ↗ P2 if PHT; holosystolic murmur in lower left parasternal region (early systolic if primary TR); murmur ↗ on inspiration (Carvallo's sign); **murmur ↗ on Mueller's maneuver**

SIGNS OF RIGHT HEART FAILURE (ascites; pulsatile liver; HSM; peripheral edema; JVD)

MANAGEMENT - SECONDARY TR: Tricuspid annuloplasty during mitral surgery in the presence of: **A)** Severe TR or **B)** Mild-to-moderate TR with dilatation of the tricuspid annulus (≥ 40 mm) or in the presence of PHT or right heart failure

MANAGEMENT - PRIMARY TR: Bioprosthesis TVR or Annuloplasty if severe symptomatic TR or severe TR with progressive RV dilatation / dysfunction or severe TR with concomitant mitral surgery

- **TR secondary to endocarditis in IDU:** total excision of the valve is possible
 ➤ **Carcinoid syndrome:** ▶▶ Chapter 5 - RCM

4.9/ PULMONARY STENOSIS

▶▶ Chapter 7 - Congenital heart disease

ETIOLOGIES: Congenital (majority)

- **Fusion of commissures:** thin, dome-shaped valve; treatment by balloon valvuloplasty
 ➤ **Dysplastic valve:** thickened leaflets; Noonan syndrome; surgical treatment

OTHER ETIOLOGIES (RARE): Carcinoid; extrinsic compression (tumor; aortic sinus aneurysm); Rheumatic; Supravalvular or subvalvular obstruction (congenital)

SEVERITY: Severe PS if peak gradient > 64 mmHg

4.10/ PULMONARY REGURGITATION

ETIOLOGIES: **A)** Annular dilatation or dilatation of PA (PHT); **B)** Endocarditis; **C)** Following correction of congenital PS - TOF; **D)** Congenital; **E)** Trauma; **F)** Carcinoid; **G)** Rheumatic; **H)** Syphilis

SEVERITY

	MILD PR (1/4)	MODERATE PR (2 TO 3/4)	SEVERE PR (4/4)
Jet envelope on continuous Doppler	Faint; Slow deceleration	Intermediate	Dense; Marked deceleration; early end of diastolic flow (\pm antegrade diastolic flow)

> **Other criteria:** D-shaped septal curvature; RV dilatation; PHT < 100 ms

PALPATION: left parasternal heave; systolic beat in the 2nd intercostal space (PA dilatation)

AUSCULTATION: Delayed P2; systolic click (PA dilatation); mid-systolic ejection murmur (\nearrow flow); right S3 and S4 (increased on inspiration)

> **Diastolic murmur:** soft, low-pitched (in the absence of PHT); \nearrow on inspiration

> **Graham Steell murmur:** decrescendo high-pitched diastolic murmur in the presence of dilatation of the pulmonary annulus secondary to PHT; accentuated P2; starts after A2; \nearrow on inspiration; signs of PHT; TR murmur

4.11/ MULTIVALVULAR HEART DISEASE

AS & MS: Aortic transvalvular gradient underestimated (low flow)

AS & MR: MR increased due to high left intraventricular pressure; the aortic transvalvular gradient can be underestimated (low flow); operate on the mitral valve when MR is severe or in the presence of significant mitral structural disease

AR & MR: MR accentuates AR causing more severe pulmonary congestion; severe LV dilatation (accentuating MR)

4.12/ VALVE PROSTHESES

MECHANICAL PROSTHESES	BIOPROSTHESES
<ul style="list-style-type: none"> • High thrombo-embolic risk • Excellent durability • Prefer in patients < 60 years 	<ul style="list-style-type: none"> • Risk of structural deterioration (Mitral >> Aortic) <ul style="list-style-type: none"> - Decreased risk in patients > 65 years • Prefer in the presence of: A) Bleeding risk; B) Difficult anticoagulation; C) > 70 years; D) Small LVOT (stentless bioprosthesis); E) Woman of childbearing potential; F) Patient preference
<ul style="list-style-type: none"> • Double-leaflet (St-Jude; Carbo-Medics; ATS Medical) • Tilting-disk (Medtronic-Hall; Omnicarbon) 	<ul style="list-style-type: none"> • Stented porcine bioprosthesis (Mosaic) • Stented bovine pericardium bioprosthesis (Carpentier-Edwards; Mitroflow) • Stentless bioprosthesis <ul style="list-style-type: none"> - Less obstructive; prefer in patients with small LVOT • Homograft: cadaveric valve <ul style="list-style-type: none"> - Used for complex aortic valve endocarditis • Ross procedure: autologous transplant of the patient's P valve to the Ao valve; use a cadaveric valve for the P valve <ul style="list-style-type: none"> - Use in young patients / women of childbearing potential • Percutaneous bioprosthesis (TAVI): <ul style="list-style-type: none"> - Deployed by balloon (Edwards-Sapien; Sapien XT) - Self-expanding bioprosthesis (Corevalve)

COMPLICATIONS: **A)** Structural deterioration; **B)** Pannus; **C)** Patient-prosthesis mismatch (►►I Chapter 1 - Echocardiography); **D)** Thrombosis; **E)** Embolism; **F)** Endocarditis (vegetation; abscess; fistula; dehiscence; destruction); **G)** Periprosthetic leak; **H)** Hemolysis related to periprosthetic regurgitation (↗ LDH; ↗ Bilirubin; ↘ Haptoglobin; Schistocytes); **I)** Dehiscence (rule out endocarditis); **J)** Bleeding secondary to anticoagulants; **K)** Pseudoaneurysm

- **Structural deterioration:** TAVI is possible (valve-in-valve)
- **Periprosthetic regurgitation:** Percutaneous closure with Amplatzer prosthesis (with 3D TEE guidance); indicated if the patient is not a candidate for surgery with significant periprosthetic regurgitation and secondary heart failure or hemolysis (transfusion-dependent); transseptal or transapical approach (M valve); retrograde arterial approach (Ao valve)

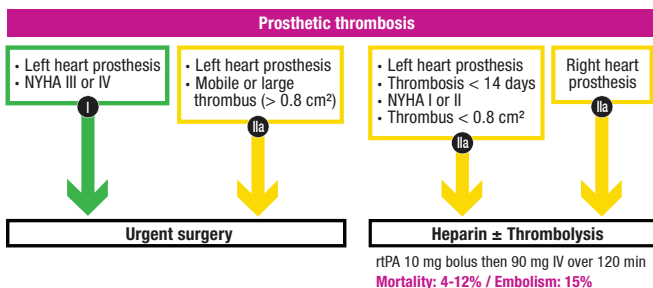
MECHANICAL VALVE: thromboembolic risk → 1-2 per 100 patient-years (aortic) and 2-3 per 100 patient-years (mitral)

PORCINE BIOPROSTHESIS: structural deterioration in 30% of patients at 10 years

- 10% at 10 years in patients > 65 years

PROSTHETIC THROMBOSIS: dyspnea; ↘ closing sound; *de novo* murmur

- **Diagnosis:** TTE - TEE - Fluoroscopy
- **Risk:** 0.1%/ year for aortic valve; 0.35%/year for mitral valve (with adequate treatment)



ANTITHROMBOTIC THERAPY

MITRAL VALVE REPAIR / ANNULOPLASTY	
<ul style="list-style-type: none"> Warfarin for 3 months (INR 2-3) ASA 80 mg qd indefinitely 	
BIOPROSTHESIS	
<ul style="list-style-type: none"> ASA 80 mg qd indefinitely ± Warfarin 3 months postoperatively (INR 2-3); Class IIa recommendation for bioprosthesis MVR; Class IIb recommendation for bioprosthesis AVR 	
MECHANICAL PROSTHESIS (MODERN)	
Low risk AVR with no risk factors* <ul style="list-style-type: none"> Warfarin indefinitely (INR 2-3) ASA 80 mg qd indefinitely 	High risk AVR with risk factors* or MVR <ul style="list-style-type: none"> Warfarin indefinitely (INR 2.5-3.5) ASA 80 mg qd indefinitely

* Risk factors: AF / LV dysfunction / History of thromboembolic disease / Hypercoagulability

EMBOLISM DESPITE WARFARIN THERAPY: **A)** If INR 2-3 → target INR 2.5-3.5; **B)** If INR 2.5-3.5 → target INR 3.0-4.0; **C)** If patient not taking ASA → add ASA

EXCESSIVE ANTICOAGULATION: **A)** Life-threatening bleeding → Prothrombin complex concentrate (or FFP) + vitamin K 5-10 mg IV (max: 1 mg/min); **B)** INR > 10 without bleeding → suspend Warfarin; vitamin K 2.5 mg PO

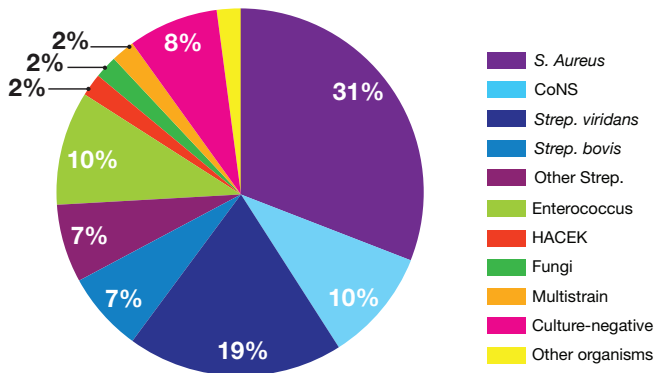
FOLLOW-UP

BIOPROSTHESIS	MECHANICAL VALVE
<ul style="list-style-type: none"> • Baseline TTE to 2-4 weeks after discharge • Annual follow-up (± TTE if new symptoms and signs) • After 10 years: annual TTE 	<ul style="list-style-type: none"> • Baseline TTE to 2-4 weeks after discharge • Annual follow-up (± TTE if new symptoms and signs)

AT FOLLOW-UP: Physical examination; ECG; CXR; ± Laboratory tests (CBC; BUN / Creatinine; Clotting assessment; INR; Blood cultures); Prophylactic antibiotics

4.13/ INFECTIVE ENDOCARDITIS

MICROBIOLOGY



Culture-negative:

Previous antibiotic; *Coxiella burnetii*; *Bartonella* sp.; *Aspergillus* sp.; *Mycoplasma pneumonia*; *Brucella* sp.; *Legionella pneumophila*; *Tropheryma whippie*; *Bartonella* sp.; Fungi (*Candida* sp.; *Aspergillus* sp.); Antiphospholipid syndrome; Marantic endocarditis; Porcine bioprosthesis allergic response; Rheumatic carditis; Polyarteritis nodosa...

<i>S. aureus</i> (including MRSA)	<ul style="list-style-type: none"> Aggressive acute endocarditis; marked toxicity Metastatic infection; valve destruction Mortality 25-40% (left heart)
Coagulase-negative Staphylococcus - CoNS (<i>S. epidermidis</i> ; <i>S. lugdunensis</i>)	<ul style="list-style-type: none"> Foreign body infection / prostheses Nosocomial infection
<i>Streptococcus viridans</i> (<i>sanguis</i>; <i>mutans</i>; <i>mitis</i>; <i>salivarius</i>...)	<ul style="list-style-type: none"> Oropharyngeal flora; alpha-hemolytic Subacute endocarditis Highly sensitive to penicillin
<i>Streptococcus bovis</i> (<i>galloyticus</i>)	<ul style="list-style-type: none"> GI flora; associated with polyps and colon cancer Subacute endocarditis Highly sensitive to penicillin
Beta-hemolytic Streptococci (groups A - B - C - G)	<ul style="list-style-type: none"> Frequent intracardiac and extracardiac complications; abscess
Enterococci (<i>faecalis</i> and <i>faecium</i>)	<ul style="list-style-type: none"> GI flora Associated with urinary tract infection/nosocomial infection Treatment requires bactericidal activity (synergism with gentamicin)
HACEK <ul style="list-style-type: none"> <i>Haemophilus sp.</i> <i>Aggregatibacter sp.</i> (previously <i>Actinobacillus</i>) <i>Cardiobacterium hominis</i> <i>Eikenella corrodens</i> <i>Kingella sp.</i> 	<ul style="list-style-type: none"> Fastidious Gram-negative bacilli Upper respiratory tract infections - Oropharyngeal flora Positive blood culture after 5 days of incubation (sometimes longer) Large vegetation
Other micro-organisms (can cause culture-negative endocarditis)	<ul style="list-style-type: none"> <i>Coxiella burnetii</i> (Q fever): subacute endocarditis; elevated IgG titer <i>Bartonella sp.</i>: Culture-negative endocarditis (perform serology or specific culture technique); cat scratch disease Fungi (<i>Candida</i>): Risk factors: immunodepression - prosthesis - central line - IDU; invasive endocarditis Others: <i>Brucella sp.</i>; <i>Tropheryma whipplei</i>; <i>Mycoplasma sp.</i>; <i>Legionella sp.</i>

RISK FACTORS

RISK FACTORS: MVP; congenital heart disease (bicuspid aortic valve; VSD; patent ductus arteriosus); rheumatic disease; degenerative valvular heart disease; IDU; prosthesis or intracardiac device; hospitalization - nursing home; central line; hemodialysis; history of endocarditis

IDU (INJECTION DRUG USERS): *S. aureus* (most frequent organism); mostly involving the tricuspid valve (look for septic pulmonary emboli)

PROSTHETIC VALVE ENDOCARDITIS (PVE)

- **Early (< 12 months post-op):** CoNS; *S. aureus*; Gram-negative bacilli; Fungi (*Candida*); *Corynebacterium sp*; *Legionella sp*
- **Late (> 12 months post-op):** similar microbiology to community-acquired native valve endocarditis
- Mortality due to *S. aureus* PVE: > 45%

MODIFIED DUKE CRITERIA

DEFINITE ENDOCARDITIS

- 2 major criteria or
- 1 major + 3 minor criteria or
- 5 minor criteria

POSSIBLE ENDOCARDITIS

- 1 major + 1 minor or
- 3 minor criteria

MAJOR CRITERIA

1. Positive blood culture

- Typical microorganism on ≥ 2 separate blood cultures
 - *Strep. viridans*; *Strep. bovis*; HACEK; *S. aureus* or
 - Community-acquired *Enterococcus* with no primary site
- Sustained bacteremia
 - **Slow method:** ≥ 2 positive blood cultures taken at an interval of ≥ 12 h or
 - **Rapid method:** 3/3 positive blood cultures or the majority of ≥ 4 blood cultures are positive (taken by different venipunctures); the first and last cultures were taken at an interval of > 1 h
- Coxiella burnetii* (Q fever): ≥ 1 positive culture bottle or IgG titer $> 1:800$

2. Endocardial involvement

- Positive echocardiography
 - Oscillating intracardiac mass (on valve or supporting structures, or in the path of regurgitant jets, or on foreign body) in the absence of an alternative explanation or
 - Abscess or
 - *De novo* prosthetic dehiscence
- De novo* valvular regurgitation

Minor criteria

- Predisposition** (heart disease or IDU)
- Fever** $\geq 38^{\circ}\text{C}$
- Vascular phenomenon:** arterial embolism; septic pulmonary infarction; mycotic aneurysm; intracranial hemorrhage; conjunctival hemorrhage; Janeway lesion
- Immunological phenomenon** (subacute endocarditis): glomerulonephritis; Osler's nodes; Roth's spot; positive rheumatoid factor; vasculitis
- Microbiological evidence:** positive blood culture but not meeting the major criterion or serological evidence of active infection (with organism consistent with infective endocarditis)

Li JS, Sexton DJ, Mick N, et al. Clin Infect Dis 2000;30:633

SYMPTOMS AND SIGNS

SYMPTOMS: fever; chills; night sweats; weight loss; dyspnea; cough; stroke; headache; nausea / vomiting; myalgia; arthralgia; retrosternal chest pain; back pain; abdominal pain; confusion

SIGNS: fever; neurological signs; signs of peripheral embolism; clubbing

- **Cardiac murmur:** in 85% of cases (uncommon in subacute endocarditis)
- **Splinter hemorrhages:** proximal nail fold; red lines
- **Petechiae:** conjunctiva; oral mucosa and palate; extremities
- **Osler's nodes:** small, painful subcutaneous nodule on fingertips (sometimes more proximal)
- **Janeway lesion:** painless, erythematous or hemorrhagic macular lesion on palms and soles
- **Roth's spot:** oval retinal hemorrhage (with central pallor)
- **Splenomegaly:** more frequent in subacute endocarditis

COMPLICATIONS

PERIPHERAL EMBOLISM

- > **Risk factors:** vegetation > 10 mm / mobile; mitral valve (anterior leaflet); *S. aureus*; *Candida*
- > **Uncommon after 2 weeks of effective treatment**
- > Stroke; digital infarction; septic arthritis; discitis; splenic or renal infarction; splenic abscess; coronary embolism; mesenteric embolism; pulmonary embolism

STROKE: A) Cardioembolic; B) Intracranial hemorrhage: ruptured mycotic aneurysm or arteritis with rupture or hemorrhagic transformation of a stroke

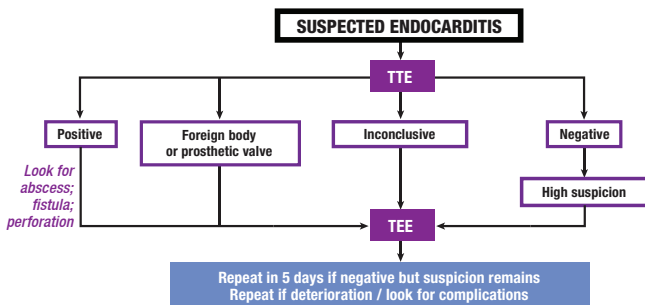
- > **Dx: A) MRI angiography or CT angiography; B) Conventional angiography** to exclude small aneurysms (< 2 mm) not seen on non-invasive imaging
- > **Indication for intervention:** progressing or ruptured aneurysm or > 7 mm
 - **Small aneurysm without rupture:** monitor (possible improvement with antibiotics)
- > **When valve surgery is indicated: A) Stroke without bleeding** → surgery **without delay** (except with extensive brain damage / coma); **B) Intracranial bleeding** → wait > 4 weeks
- > **Management of anticoagulation:** stop anticoagulation in patients with mechanical valve > 2 weeks in the presence of stroke (class IIa recommendation)

HEART FAILURE: A) Valve destruction; B) Ruptured chordae tendineae; C) Fistula; D) Purulent myocarditis; E) Coronary embolism; F) Valve obstruction

ARF: A) Immune complex glomerulonephritis (↓ complement); **B) Renal embolism** (renal infarction); **C) Prerenal ARF; D) Gentamicin toxicity; E) Interstitial nephritis** (secondary to antibiotics)

AV BLOCK / CONDUCTION DISORDERS: perivalvular abscess

ECHOCARDIOGRAPHY



SENSITIVITY: TTE → 70% (50% for prosthesis); **TEE** → 96% (92% for prosthesis)

VEGETATION: Oscillating mass with independent movement; atrial aspect for M and T valves; ventricular aspect for Ao and P valves; on the surface of implanted intracardiac material

- > **DDx:** Old vegetation; Non-bacterial thrombotic endocarditis (marantic); Antiphospholipid syndrome / SLE (Libman-Sacks); degenerative changes / myxomatous valve; Lambli's excrescences; ruptured chordae tendineae; Ca^{2+} ; nodule - RA; thrombus; fibroelastoma

LOOK FOR: vegetation; abscess (not communicating with the lumen) / **pseudoaneurysm** (pulsatile; colour-Doppler flow detected); **prosthetic dehiscence** (± rocking motion); valvular aneurysm (saccular bulging); intracardiac fistula; valve perforation - channel; purulent pericarditis; obstruction; early mitral valve closure in acute AR (with restrictive diastolic pattern)

MANAGEMENT

ANTIBIOTIC TREATMENT: Target → eradication of microorganisms; bactericidal antibiotic action; sufficient serum concentrations (to penetrate the vegetation by diffusion); minimal toxicity

- > **MIC:** Minimum inhibitory concentration (to inhibit growth)
- > **MBC:** Minimum bactericidal concentration (to reduce the inoculum)

DURATION: from the first day on which blood cultures are negatives

- > **Positive operative tissue cultures:** entire antimicrobial course after valve surgery

PNC-SENSITIVE *STREP. VIRIDANS* OR *STREP. BOVIS* - MIC < 0.12 µG/ML

PNC G	12-18 million U / day IV (4-6 doses)	4 weeks
Ceftriaxone	2 g / day IV or IM (1 dose)	4 weeks
PNC G (or Ceftriaxone) + Gentamicin	12-18 million U / day IV (4-6 doses) 3 mg/kg / day IV or IM (1 dose)	2 weeks 2 weeks
Vancomycin	30 mg/kg / day IV (2 doses)	4 weeks

- **Prosthesis: A)** 6 weeks therapy of PNC G (24 million U / day) or Ceftriaxone (with or without gentamicin for the first 2 weeks); **B)** 6 weeks therapy of Vancomycin
- Serum Vancomycin levels: trough 10-15 µg/mL
- Serum Gentamicin levels (3 divided doses): peak serum 3-4 µg/mL; trough < 1 µg/mL

STREP. VIRIDANS OR *STREP. BOVIS* RELATIVELY RESISTANT - MIC 0.12 – 0.50 µG/ML

PNC G + Gentamicin	24 million U / day IV (4-6 doses) 3 mg/kg / day IV or IM (1 dose)	4 weeks 2 weeks
Vancomycin	30 mg/kg / day IV (2 doses)	4 weeks

- **Prosthesis:** 6 weeks therapy
- Ceftriaxone: consider as an alternative if the isolate is susceptible

METHICILLIN-SENSITIVE *STAPHYLOCOCCUS* - NO FOREIGN BODY

Cloxacillin	12 g / day IV (4-6 doses)	6 weeks
Cefazolin	6 g / day IV (3 doses)	6 weeks
Vancomycin (β-lactam allergy evaluation)	30 mg/kg / day IV (2 doses)	6 weeks

- Uncomplicated right heart endocarditis: 2 weeks

METHICILLIN-RESISTANT *STAPHYLOCOCCUS* - NO FOREIGN BODY

Vancomycin	30 mg/kg / day IV (2 doses)	6 weeks
Daptomycin	≥ 8 mg/kg / day IV (1 dose)	6 weeks

METHICILLIN-SENSITIVE *STAPHYLOCOCCUS* - PROSTHESIS

Cloxacillin + Rifampicin + Gentamicin	12 g / day IV (4-6 doses) 900 mg / day IV or PO (3 doses) 3 mg/kg / day IV or IM (2-3 doses)	≥ 6 weeks ≥ 6 weeks 2 weeks
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METHICILLIN-RESISTANT *STAPHYLOCOCCUS* - PROSTHESIS

Vancomycin + Rifampicin + Gentamicin	30 mg/kg / day IV (2 doses) 900 mg / day IV or PO (3 doses) 3 mg/kg / day IV or IM (2-3 doses)	≥ 6 weeks ≥ 6 weeks 2 weeks
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- Rifampin: caution in relation to multiple drug interactions

ENTEROCOCCUS SPP.		
Ampicillin + Gentamicin	2 g IV every 4 h 3 mg/kg / day IV or IM (2-3 doses)	4-6* weeks 2-6 weeks (6 weeks with prosthetic valve)
Ampicillin + Ceftriaxone (<i>E. faecalis</i>)	2 g IV every 4 h 4 g / day IV or IM (2 doses)	6 weeks 6 weeks
Vancomycin + Gentamicin	30 mg/kg / day IV (2 doses) 3 mg/kg / day IV or IM (3 doses)	6 weeks 6 weeks

* 4 weeks with < 3 months duration of symptoms (6 weeks with ≥ 3 months)

HACEK		
Ceftriaxone	2 g / day IV or IM (1 dose)	4 weeks (6 weeks if prosthesis)

EMPIRICAL TREATMENT (BEFORE PATHOGEN IDENTIFICATION) – COMMUNITY-ACQUIRED NATIVE VALVE OR LATE PROSTHETIC VALVE (> 12 MONTHS)		
Ampicillin + Cloxacillin + Gentamicin	2 g IV every 4 h 12 g / day IV (4-6 doses) 3 mg/kg / day IV or IM	
EMPIRICAL TREATMENT (BEFORE PATHOGEN IDENTIFICATION) – EARLY PROSTHETIC VALVE (< 12 MONTHS) OR NOSOCOMIAL ENDOCARDITIS		
Vancomycin + Gentamicin + Rifampin	30 mg/kg / day IV (2 doses) 3 mg/kg / day IV or IM 900 mg / day IV or PO (3 doses)	

PROPHYLACTIC ANTIBIOTICS

Candidates

- Prosthetic valve (or prosthetic valve material)
- History of infective endocarditis
- Congenital heart disease
 - Unrepaired cyanotic heart disease (including palliative conduits and shunts)
 - Complete repair with prosthetic material < 6 months
 - Repair with residual defect close to prosthesis / patch (preventing endothelialization)
- Transplant recipient with regurgitation on a structurally abnormal valve

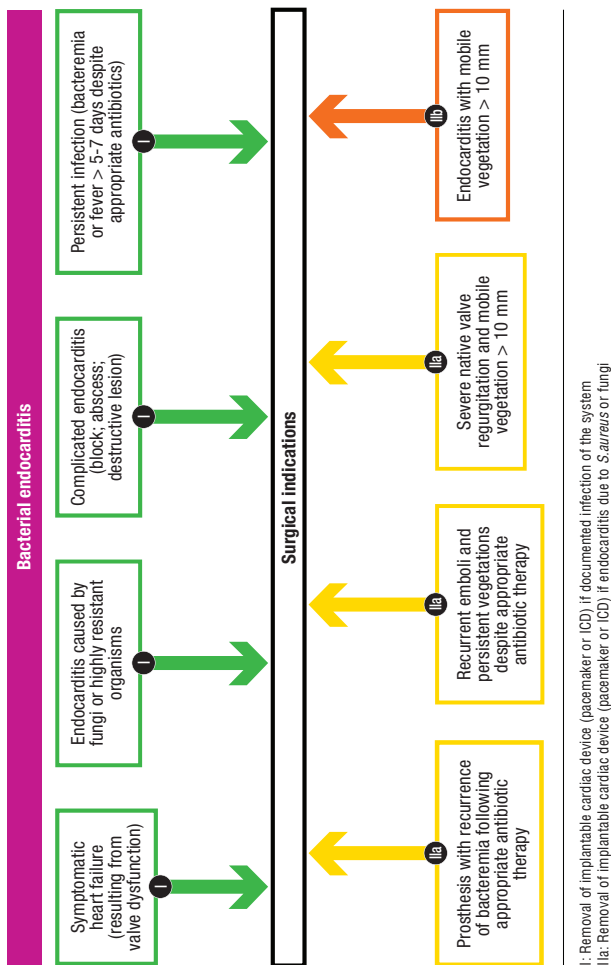
Procedure

- Dental procedure involving the gums or periapical region of the tooth or perforation of the oral mucosa

- Amoxicillin 2 g PO** (60 min before the operation) or
- Cephalexin 2 g PO or Azithromycin 500 mg PO or Clindamycin 600 mg PO or
- Cefazolin or Ceftriaxone 1 g IM or IV

SURGICAL INDICATIONS

- Coronary CT angiography can provide coronary artery evaluation before cardiac surgery



4.14/ CARDIAC IMPLANTABLE ELECTRONIC DEVICE INFECTION

MICROBIOLOGY: CoNS (42%); Sensitive *S. aureus* (25%); MRSA (4%); Gram-negative bacilli (9%); Multistain (7%); Culture-negative (7%)

PATHOGENESIS

A) Pocket infection (during procedure or secondary to skin erosion) → ± propagation of infection to intravascular leads → ± intracardiac propagation of infection

B) Bacteremia (*S. aureus*) → hematogenous pocket and/or lead infection

ASSESSMENT: blood cultures x 2; TEE if blood cultures positive (rule out vegetation adherent to the lead and/or the valve); culture of the pocket after explantation of the system; FDG PET-CT (rule out increased FDG uptake)

MANAGEMENT

A) Superficial skin infection without involvement of the pocket and system → oral antibiotics against *Staphylococcus* for 7 to 10 days

B) Pocket infection and/or skin erosion: complete removal of the system (even in absence of systemic infection) + ATB

C) Documented system infection (lead endocarditis and/or valve endocarditis and/or bacteremia with pocket involvement): complete removal of the system + ATB (risk of clinically significant pulmonary embolism during percutaneous lead removal if vegetation on electrode > 2 cm)

D) Valve endocarditis (without documented system infection): complete removal of the system (± implantation of a new epicardial system) + ATB

E) Occult *Staphylococcus* bacteremia: complete removal of the system + ATB

EMPIRICAL ANTIBIOTICS: Vancomycin (then according to the organism / sensitivity)

DURATION OF ANTIBIOTICS: **A)** 7-10 days if skin erosion with no inflammatory changes;

B) 10-14 days if pocket infection; **C)** > 2-4 weeks IV if bacteremia (repeat TEE in 2 weeks in the case of lead vegetation); **D)** > 4-6 weeks if complication (valve endocarditis; septic thrombophlebitis; osteomyelitis)

OPTIMAL TIMING FOR PLACEMENT OF A NEW DEVICE (CONTRALATERAL): **A)** Skin erosion / Pocket infection: in the absence of bacteremia; **B)** Positive blood cultures: absence of bacteremia x > 72 h post-explantation; **C)** Valve endocarditis: wait > 14 days before reimplanting an endovenous system

TEMPORARY PACEMAKER: Use active fixation lead

4.15/ RHEUMATIC FEVER

Autoimmune reaction 2 to 4 weeks after group A beta-hemolytic *Streptococcus* sore throat (*S. pyogenes*)

JONES' CRITERIA

Major criteria

- 1) Carditis and valvulitis
- 2) Migratory arthritis (swollen joints)
- 3) Sydenham's chorea (CNS inflammation; late manifestation)
- 4) Erythema marginatum (trunk; proximal limbs)
- 5) Subcutaneous nodules

Minor criteria

- Arthralgia
- Fever
- Elevation of inflammatory markers (ESR - CRP)
- Prolonged PR

Diagnosis: group A Streptococcal sore throat followed by:

- 2 major criteria or
- 1 major criterion + 2 minor criteria

CARDITIS

PANCARDITIS: Valvulitis (MR >> AR); LV dysfunction; pericarditis

PHYSICAL EXAMINATION (IN A CONTEXT OF ACUTE RHEUMATIC FEVER):

Tachycardia; ↓ S1; ↑ P2 in the case of severe MR; S3; holosystolic murmur; **Carey Coombs murmur** (mid-diastolic murmur secondary to turbulence and increased mitral diastolic flow); early diastolic decrescendo murmur in the case of AR; pericardial friction rub; TR murmur

LONG-TERM SEQUELAE: Progressive mitral valve disease (MS >> MR) which becomes symptomatic after several decades; Ao or T valve involvement is possible

PRIMARY PREVENTION

Start antibiotics < 10 days after onset of sore throat

PNC V 500 mg PO bid for 10 days

SECONDARY PREVENTION

Candidate	Agent	Duration
All patients with history of rheumatic fever (with or without carditis) due to the high risk of recurrence (class I recommendation)	<ul style="list-style-type: none"> • PNC G 1.2 million U IM every 4 weeks (or every 3 weeks if residual cardiac lesion) or • PNC V 200 mg PO bid or • Sulfadiazine 1 g PO daily 	<ul style="list-style-type: none"> • Persistent valvular heart disease: > 10 years since last episode (until age of 40 years minimum; long term if in contact with children) • History of carditis but no sequelae: > 10 years since episode (until age of 21 years minimum) • Absence of carditis: > 5 years since episode (until age of 21 years minimum)

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Diseases of the Pericardium & Myocardium

05

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5.1/ DISEASES OF THE PERICARDIUM: ETIOLOGIES

IDIOPATHIC (MOST COMMON)

INFECTIOUS

- **Viral:** echovirus; coxsackievirus; adenovirus; EBV; CMV; HCV; HIV; influenza; parvovirus B19
- **Bacterial:** Pneumococcus; Staphylococcus; Streptococcus; Mycoplasma; Lyme; *Haemophilus influenzae*; Meningococcus; Gonococcus; *Coxiella burnetii*; *Legionella* spp; *Listeria* spp
- **Mycobacteria:** *M. tuberculosis*; *M. avium*
- **Fungi:** histoplasmosis; coccidioidomycosis
- **Parasites:** toxoplasmosis; echinococcosis
- **Infective endocarditis** (extension)

INFLAMMATORY - IMMUNE

- **Collagen diseases:** SLE; RA; Scleroderma; Sjögren
- **Vasculitis:** PAN; Giant cell arteritis; Churg-Strauss; Takayasu; Behçet
- Sarcoidosis
- Still disease
- **Dressler's syndrome:** late post MI or late post-cardiac surgery or late post-trauma
- Myopericarditis
- Inflammatory bowel disease
- Acute rheumatic fever (pancarditis)
- **Medications:** Procainamide; Hydralazine; Cyclosporine; Doxorubicin; Cyclophosphamide...

NEOPLASTIC

- **Primary:** mesothelioma; angiosarcoma; lipoma; paraganglioma
- **Secondary:** Lung; Breast; Lymphoma; Kaposi sarcoma; GI carcinoma; melanoma; sarcoma...

RADIOTHERAPY

EARLY POST-MYOCARDIAL INFARCTION (2-4 DAYS)

EARLY POST-CARDIAC SURGERY

HEMOPERICARDIUM

- Trauma
- Free wall rupture (infarction)
- Aortic dissection
- **Iatrogenic:** PCI; pacemaker; ablation of arrhythmia; ASD closure; valve repair / replacement; endomyocardial biopsy

TRAUMA

- Contusion; Penetrating injury; Post-CPR

CONGENITAL

- Cyst
- Congenital absence of pericardium

OTHER

- Renal failure - Uremia
- Dialysis
- Anorexia nervosa
- Chylopericardium
- Hypothyroidism or Hyperthyroidism
- Amyloidosis
- Heart failure (transudate)
- Severe PHT (transudate)
- Familial Mediterranean fever; TRAPS syndrome

SPECIFIC ENTITIES

EARLY POST-MI PERICARDITIS (< 1 WEEK): extension of transmural necrosis to the pericardium (with localized pericarditis); **localized ST elevation; look for ventricular rupture** if effusion associated; treatment with ASA 650 mg PO qid at tapered doses (avoid other NSAIDs) + Colchicine

DRESSLER'S SYNDROME: Late post-MI or post-cardiac surgery or post-trauma pericarditis; **autoimmune phenomenon;** polyserositis; fever; treatment with NSAID + Colchicine

RADIATION-INDUCED PERICARDITIS: A) Acute; B) Late: several months to several years; pericarditis - effusion - constriction - effusion / constriction

METASTATIC PERICARDIAL EFFUSION: Management → pericardiocentesis with drainage; intrapericardial chemotherapy or sclerosing agent; radiotherapy; pericardial window (surgical via left minithoracotomy or percutaneous approach)

CHRONIC PERICARDIAL EFFUSION: **Look for and treat an underlying cause;** look for systemic inflammation (CRP); **when idiopathic** → monitor by regular TTE **vs.** trial of NSAID / colchicine **vs.** pericardiocentesis (if chronic and > 20 mm; if symptomatic; if suspicion of bacterial or neoplastic aetiology)

DIALYSIS-ASSOCIATED PERICARDITIS: Now more frequent than uremic pericarditis; occurs even with normal plasma urea; consider intensifying dialysis

BACTERIAL PERICARDITIS: Direct extension of pneumonia or endocarditis or hematogenous spread or iatrogenic; **toxic patient;** urgent pericardiocentesis / urgent surgical drainage (± pericardiotomy; ± pericardiectomy)

5.2/ ACUTE PERICARDITIS

Inflammation of the pericardium

Dry vs serous vs fibrinous pericarditis (fibrin; granulation; adhesions; scarring) vs suppurative (bacterial) vs hemorrhagic

PRESENTATION: Retrosternal chest pain (**pleuritic; radiation to trapezius; worse in supine position; relieved by sitting forward**); dyspnea

CLINICAL FEATURES: ± fever; ± tachycardia; ± signs of tamponade

- **Pericardial friction rub: 1 or 2 or 3 components (systole; rapid ventricular filling; atrial kick);** evanescent; left parasternal region; patient seated, leaning forward in forced expiration

+

ECG: 4 phases

1. Diffuse ST elevation (concave); PR segment depression; mirror changes in aVR
2. Normalization of ST segment with depression of the J point
3. T wave inversion
4. T wave normalization

ASSESSMENT: ECG; TTE; Creatinine - BUN; CBC; liver tests; CXR; ESR - CRP; Troponin (if ⚠: consider myopericarditis or MI)

- ± ANA; ANCA; RF; PPD; HIV; HCV; TSH; BNP; tumor work-up; chest CT scan and/or cardiac MRI; Ferritin (Still disease); ACE (Sarcoidosis); Serology for *Coxiella burnetii* or for Lyme disease
- ± Pericardial aspiration (looking for cancer cells - cytology; cultures / mycobacterium culture; PCR for TB; Adenosine deaminase); Biopsy (cancer; TB)

DIAGNOSIS: Clinical diagnosis: ≥ 2 out of 4 criteria

Pleuritic and positional retrosternal chest pain	Pericardial friction rub (pathognomonic)	Typical ECG changes	Pericardial effusion
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MANAGEMENT

IBUPROFEN 600 to 800 mg every 6 to 8 h  **10 to 14 days (with tapering based on clinical response)**

/or
ASA 650 mg PO qid



PPI daily



COLCHICINE 0.5 mg bid for 3 months if > 70 kg (0.5 mg daily if < 70 kg)
(★ COPE and ★ ICAP studies)

- > Look for and treat any specific cause
- > Analgesia - Narcotics PRN
- > Rest / avoid exercise until complete resolution of symptoms (athletes: 3 months)
- > **Corticosteroids: not recommended as first-line therapy**, as risk factor for recurrence
- > **Hospitalization:** **A)** Fever; **B)** Subacute course; **C)** Failure to respond within 7 d to NSAID; **D)** Large pericardial effusion (> 20 mm) and/or tamponade; **E)** Myopericarditis; **F)** Trauma; **G)** Underlying cause; **H)** Immunosuppression; **I)** Receiving anticoagulant

COMPLICATIONS: pericardial effusion; tamponade; constriction

5.3/ INCESSANT AND RECURRENT PERICARDITIS

INCESSANT PERICARDITIS: recurrence of symptoms on withdrawal of treatment

RECURRENT PERICARDITIS: new episode after a symptom-free interval of > 4 -6 weeks

- > "Self-reactivity" sometimes develops following the first episode

MANAGEMENT

1. Rule out a specific cause
2. Resume NSAID with tapering over > 12 weeks; assess the response to therapy with CRP
3. Colchicine (★ CORP; ★ CORP-2) for ≥ 6 months
4. Avoid corticosteroids (in case of contraindications to ASA / NSAID / Colchicine \rightarrow Prednisone 0.2-0.5 mg/kg daily for several weeks then gradual tapering)
5. Last resort: Azathioprine; IV immunoglobulins; anti-IL-1 (e.g. Anakira); Pericardiectomy

5.4/ CARDIAC TAMPONADE

THE PERICARDIUM is a closed sac with a low volume reserve; accumulation of fluid induces increased intrapericardial pressure and **compression of the heart chambers** ($R > L$)

- > **Normal volume of pericardial fluid:** < 50 mL

Increase then equalization of diastolic pressures in heart chambers \approx **INTRAPERICARDIAL PRESSURE** ≈ 15 -20 mmHg

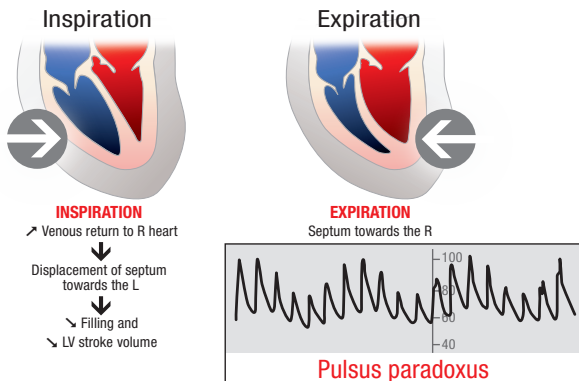
CLINICAL FEATURES: tachypnea; tachycardia; diaphoresis; signs of hypoperfusion

- > **Beck's triad:** hypotension; muffled heart sounds; **JVD**
- > **Jugular:** attenuated y descent



PULSUS PARADOXUS: $\searrow > 10$ mmHg of SBP on inspiration

- > Difference between the two pressures on sphygmomanometry when:
 1. Onset of Korotkoff sounds (expiration only)
 2. Korotkoff sounds are audible throughout the respiratory cycle
- > **Pathophysiology:** cardiac transmission of respiratory variations of intrathoracic pressure is maintained



- > **Tamponade and absence of pulsus paradoxus:** AR; ASD; severe LV dysfunction; LVH; RVH; severe hypotension; pericardial adhesions; localized effusion
- > **DDx of pulsus paradoxus:** constrictive pericarditis (effusion-constriction); pulmonary embolism; RV infarction; pulmonary disease with marked variations of intrathoracic pressure (asthma; COPD; OSAHS); obesity; ascites; severe hypotension / hemorrhage; pectus excavatum

ECG: low voltage; electrical alternans

CXR: rounded and enlarged heart shadow

FLUOROSCOPY: abolition of cardiac pulsation

TTE: pericardial effusion (anterior to aorta on PLAX); **RA collapse during its relaxation** after the peak of the R wave (very sensitive and specific if $> 1/3$ of cardiac cycle); **early diastolic RV collapse after T wave** (absent if RVH); abnormal respiratory movement of the septum; plethoric IVC

> **Exaggerated respiratory variations of transvalvular flow**

- Measure the first E wave following the start of inspiration and expiration
- **Mitral valve:** \searrow E on inspiration; variation $> 30\%$ ($E_{exp} - E_{insp} / E_{exp}$)
- **Tricuspid valve:** \searrow E on expiration; variation $> 60\%$ ($E_{exp} - E_{insp} / E_{exp}$)

> **Pulmonary veins:** predominance of **systolic** flow (\searrow Y wave)

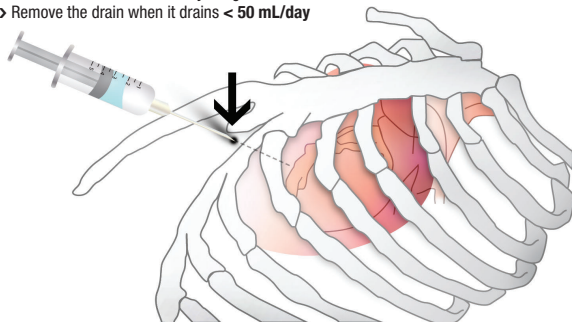
> **Hepatic veins:** expiration \rightarrow \searrow antegrade flow and \nearrow diastolic reversal (A wave)

	TAMPONADE	CONSTRICTION
Pulsus paradoxus	Present	Possible (1/3)
Jugular	Attenuation of Y wave	Prominent Y wave "M or W" Pattern
Effect of inspiration on CVP	Reduction (normal effect)	Kussmaul (increase or absence of reduction)

	TAMPONADE	CONSTRICTION
Equalization of diastolic pressures	+	+
Square root sign (ventricular curve)	Absent	+
Ventricular interdependence (discordance of RV and LV systolic pressures during breathing)	Present	Present
Valve flow variations	<ul style="list-style-type: none"> • M valve: \searrow E on inspiration; variation > 30 % • T valve: \searrow E on expiration; variation > 60 % 	<ul style="list-style-type: none"> • M valve: \searrow E on inspiration; variation > 25 % • T valve: \searrow E on expiration; variation > 40 %
Pulmonary vein flow	Systolic	Diastolic
Hepatic vein flow	\nearrow Diastolic reversal on expiration	\nearrow Diastolic reversal on expiration

PERICARDIOCENTESIS

1. Patient in 45° supine; subxyphoid approach (1 cm below the xyphoid process and 1 cm to the patient's left); local anesthesia
2. Needle introduced at an angle of 30-45° to the skin aiming for the left scapula while applying negative pressure on the syringe (\pm echocardiographic guidance)
3. Confirm the correct position of the needle: contrast in the case of echocardiographic guidance; insertion of a guide into the pericardial sac in the case of fluoroscopic guidance
4. Insertion of a dilator followed by a Pigtail catheter
 > Remove the drain when it drains < 50 mL/day



- > **Indications: A)** Tamponade; **B)** Diagnosis of pericardial effusion (metastases; bacterial pericarditis; TB)
- > **Contraindication:** Aortic dissection with hemopericardium; ventricular rupture; coagulopathy; inaccessible effusion
- > **Complications (1-2%):** Perforation of right heart chambers; coronary laceration; pneumothorax; hepatic puncture; arrhythmia; arterial bleeding
- > **Surgical drainage:** Following trauma or ventricular rupture or loculated / organized effusion or when biopsy is required or bacterial pericarditis
- > **Pericardial window (pericardiotomy):** During reaccumulation / frequent recurrence; surgical or balloon

5.5/ CONSTRICTIVE PERICARDITIS

Pericardial fibrosis / calcification / adhesions

ETIOLOGIES: Idiopathic; Postoperative; Viral pericarditis; Recurrent pericarditis; Post-radiotherapy; TB; Other (infectious; neoplastic; collagen disease; uremia; post-trauma; sarcoidosis)

CONSEQUENCE: limited filling of heart chambers

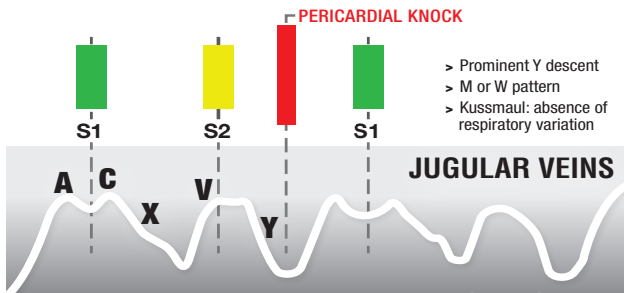
- Rapid early diastolic ventricular filling (prominent Y wave), which then ceases abruptly at mid-diastole (rigid pericardium)

PRESENTATION: systemic venous congestion mimicking right heart failure

CLINICAL FEATURES: JVD; prominent Y wave (normal X descent; "M or W" pattern);

Kussmaul's sign (increase or absence of decrease of CVP on inspiration); \pm pulsus paradoxus (especially in the case of effusion - constriction); anasarca; hepatomegaly; pulsatile liver; signs of liver disease; jaundice; cardiac cachexia; low output state

- **Pericardial knock:** high-pitched early diastolic sound at the apex or left parasternal region corresponding to the abrupt cessation of ventricular filling (\pm palpable)
- **DDx of Kussmaul's sign:** RV infarction; pulmonary embolism; RCM; TS; RA tumor; severe right heart failure



CXR: Pericardial calcifications

CT SCAN AND MRI: pericardial thickening > 4 mm (20% of patients have normal thickness); calcifications (CT scan); pericardial adhesions to the myocardium (MRI)

TTE: abrupt cessation of ventricular filling at early diastole; abnormal respiratory movement of the septum (septal bounce); restrictive ventricular filling pattern; plethoric IVC

➤ **Exaggerated respiratory variations of transvalvular flow**

- Measure the first E wave following the start of inspiration and expiration
- **Mitral valve:** \searrow E on inspiration; variation $> 25\%$ ($E_{exp} - E_{insp} / E_{exp}$)
- **Tricuspid valve:** \searrow E on expiration; variation $> 40\%$ ($E_{exp} - E_{insp} / E_{exp}$)

- Variations masked if \nearrow LA pressure (unmasked by asking the patient to sit up)
- **DDx:** RV infarction; pulmonary embolism; pleural effusion; COPD (COPD: \nearrow SVC antegrade systolic flow velocity > 20 cm/s on inspiration)

➤ **Pulmonary veins:** predominance of diastolic flow (\nearrow Y wave)

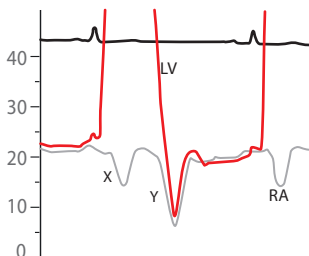
➤ **Hepatic veins:** expiration \rightarrow decreased antegrade flow and increased diastolic reversal (A wave)

➤ **Tissue Doppler imaging of septal mitral annulus:** $E' > 8$ cm/s (annulus paradoxus)

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Diseases of the Pericardium & Myocardium

CARDIAC CATHETERIZATION

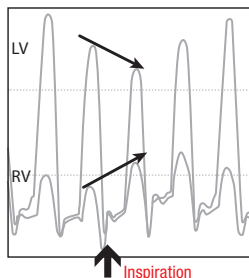


ATRIAL CURVE:

- Prominent Y descent
- W or M pattern
- Kussmaul

VENTRICULAR CURVE:

- Square root sign



VENTRICULAR CURVES:

- Equalization of end-diastolic pressures
- Respiratory discordance of ventricular systolic pressures

> **Ventricular curve: square root sign:** rapid initial ventricular filling, then increase and equalization of end-diastolic pressures of the chambers (≈ 20 mmHg)

- $LVEDP - RVEDP < 5$ mmHg

- Can be detected with a bolus in the presence of dehydration

> **Interdependence:** RV and LV systolic pressure discordance during respiration

INSPIRATION

- ↓ Intrathoracic pressure
- ↓ Pulmonary venous pressure

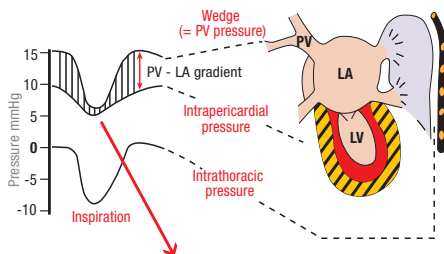
(no change of intrapericardial pressure and LA pressure)



↓ ↓ PV - LA PRESSURE GRADIENT

=

↓ venous return to LV (septum shifted to the left)



Absence of transmission of respiratory intrathoracic pressure variations to the intrapericardial compartment (isolated by the thickened pericardium)

Adapted from: Bunnell IL, Holand JF, Griffith GT, Greene DG. Hemodynamics during induced cardiac tamponade in man. *Am J Med* 1960;25:640-6

MANAGEMENT

1. Diuretics (beware of decreased preload)
2. Avoid BB-CCB (compensatory tachycardia to maintain cardiac output)
3. **Pericardiectomy:** the only definitive treatment (perioperative mortality: 5-15%)
4. NSAID in acute effusive / constrictive pericarditis

5.6/ CONGENITAL ANOMALIES OF THE PERICARDIUM

PERICARDIAL CYST

Often adjacent to right chambers

Cardiac MRI PRN; Conservative management (except when compressive)

CONGENITAL ABSENCE OF THE PERICARDIUM

Most often partial absence of the left pericardium

COMPLICATIONS: hernia / strangulation of part of the heart; retrosternal chest pain - syncope - sudden death

ECG: Incomplete RBBB; poor precordial progression of R wave

CXR: Marked levoposition; loss of right heart contour; interposition of lung between Ao and main PA

TTE: Unusual imaging window (PLAX); RV appears dilated; exaggerated heart movements; abnormal movement of interventricular septum

CARDIAC MRI: Marked levoposition; presence of lung parenchyma between Ao and main PA and between inferior heart surface and diaphragm; \pm hernia of part of the heart

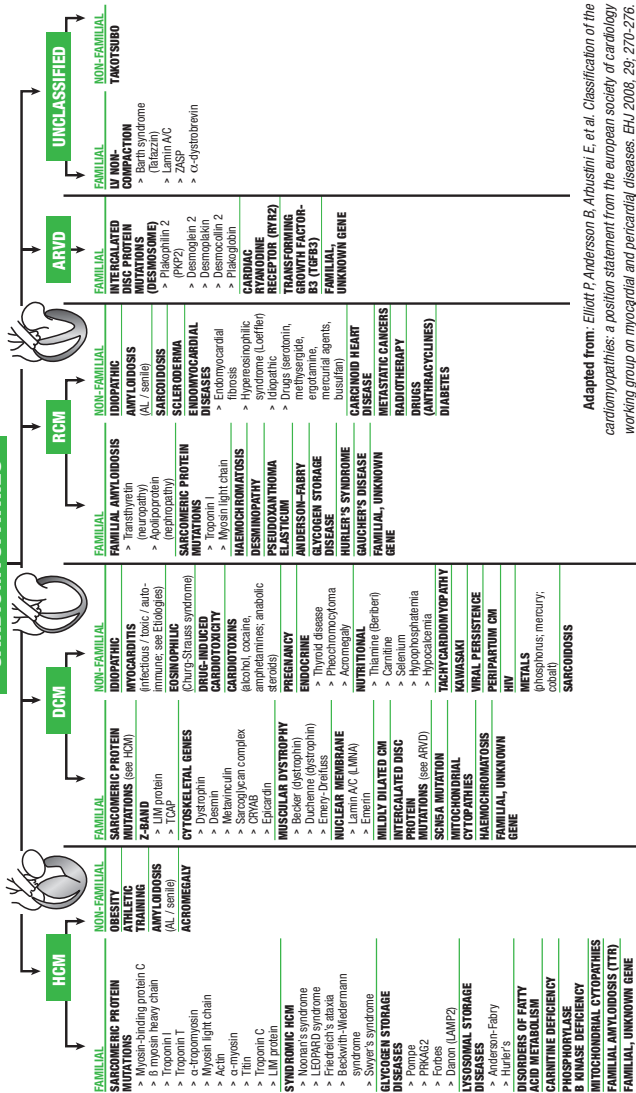
TREATMENT: Pericardioplasty (in the presence of symptoms or hernia)

5.7/ CARDIOMYOPATHIES - CLASSIFICATION

Myocardial disease (abnormal structure and function) in the absence of CAD - HTN - valvular heart disease - congenital heart disease

►►I Classification (following page)

CARDIOMYOPATHIES



Adapted from: Elliott P, Andersson B, Arbustini E, et al. Classification of the cardiomyopathies: a position statement from the European Society of Cardiology working group on myocardial and pericardial diseases. *EHJ* 2008; 29: 270-276.

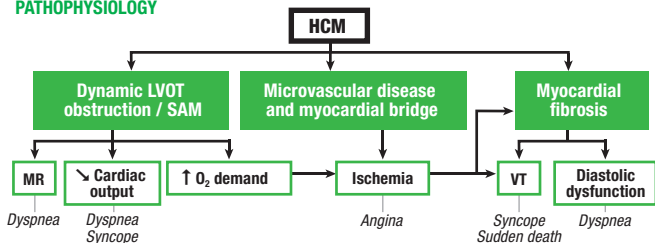
5.8/ HYPERTROPHIC CARDIOMYOPATHY

LV hypertrophy without dilatation and with no identifiable cause (see DDx)

Obstructive HCM (intraventricular gradient at rest or on exercise) versus non-obstructive HCM (gradient < 30 mmHg)

Autosomal dominant; sarcomere protein gene

PATHOPHYSIOLOGY



DIFFERENTIAL DIAGNOSIS

- Valvular heart disease; subaortic membrane; HTN (regression of LVH with tight blood pressure control); amyloidosis (TTR; AL); CRF; isolated basal septal hypertrophy in the elderly; acromegaly; pheochromocytoma
- Syndromic: Noonan; LEOPARD; Friedreich's ataxia
- Glycogen storage disease; Lysosomal storage disease (Anderson-Fabry); Mitochondrial cytopathy
 - Symmetrical LVH; WPW (Danon and PRKAG2)
- High-level athlete

	ATHLETE	HCM
Genetic test or family history	Negative	Positive
Diastolic dysfunction	Absent	Present
LV end-diastolic diameter	> 55 mm	< 45 mm
SAM	Absent	Present
Asymmetrical LVH	Absent	Present
Severe LVH (> 17 mm)	Absent	Present
Regression of LVH after stopping training	Present	Absent
VO ₂ max > 110% predicted	Present	Absent
Scar / fibrosis on MRI	Absent	Present

PRESENTATION: dyspnea; retrosternal chest pain; syncope; AF; malignant arrhythmia; sudden death

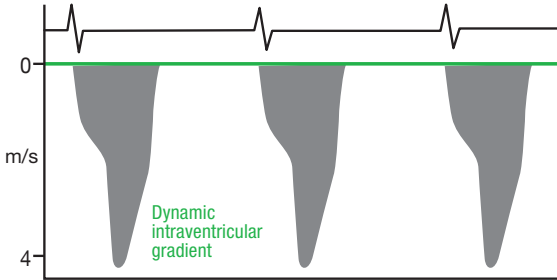
- Progression to DCM with systolic dysfunction ("burn-out" HCM): < 5%

CLINICAL FEATURES: rapid carotid upstroke with **pulsus bisferiens** ("spike and dome"); **3 components at apex** (early systolic wave; late systolic wave; S4); paradoxical split S2; **left parasternal systolic ejection murmur** (↑ on Valsalva or on standing); MR murmur (radiation to axilla)

ECG: LVH; LAH; T - ST abnormalities (diffuse T wave inversion in apical HCM); Q waves; arrhythmias

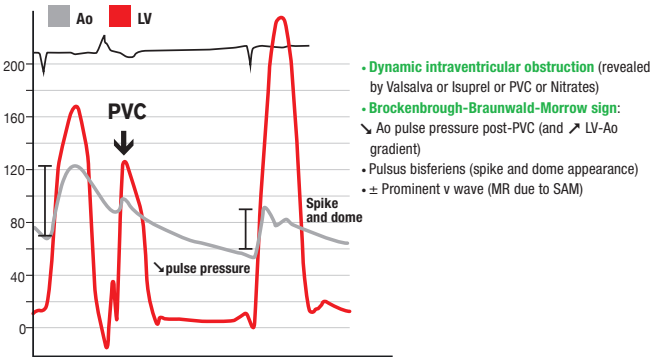
TTE (± CONTRAST): **A)** LV wall ≥ 15 mm (that is not explained solely by loading conditions); asymmetrical septal hypertrophy (septum / posterior wall $> 1.5:1$) and/or apical hypertrophy and/or anterolateral hypertrophy or concentric; \nearrow LV mass; **B)** SAM (mid-to-late systolic MR with posterior jet); **C)** Dynamic intraventricular gradient ≥ 30 mmHg amplified by Valsalva maneuver (continuous Doppler shows a **late-peaking dagger-shaped appearance**); **D)** Diastolic dysfunction; **E)** Structural abnormality of the mitral valve (elongated leaflets; abnormal insertion of anterolateral papillary muscle); **F)** LA dilatation; **G)** Apical aneurysm

\rightarrow **Exercise echocardiography:** in symptomatic patients to detect a significant dynamic intraventricular gradient (≥ 50 mmHg) when absent at rest



\rightarrow **DDx of Dynamic intraventricular gradient:** Takotsubo; cardiac amyloidosis; anterior myocardial infarction (basal hyperdynamism); post-AVR (AS with LVH); sigmoid septum in elderly people; hypertensive heart disease; small hyperdynamic LV

CARDIAC CATHETERIZATION



STRESS TEST: evaluate functional capacity; look for abnormal BP response (\searrow BP > 20 mmHg $+$ or absence of increase of BP > 20 mmHg); combine with echocardiography to demonstrate dynamic obstruction; repeat stress test every 2-3 years in clinically stable patients

CARDIAC MRI: LVH; Rule out apical HCM; late gadolinium enhancement (interventricular septum; free wall; RV insertion sites) with $\geq 10\%$ of LV mass associated with increase SCD risk $+$

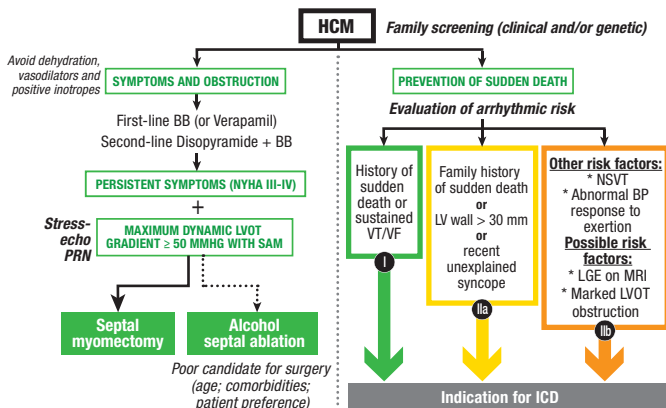
BIOPSY: disorganized myocyte architecture; interstitial fibrosis

GENETIC TEST: indicated routinely (Class I); enables cascade genetic screening of the relatives; positive in 60-70% of cases

MANAGEMENT

- Avoid strenuous exertion / competitive sports
- **Hypotension due to LVOT obstruction:** volume; BB; Phenylephrine
- **Anticoagulation** for AF irrespective of CHADSVASc score
- **Family screening:** 1st degree relatives; clinical and/or genetic screening

12 - 18 YEARS OR COMPETITIVE SPORTSMAN	> 18 YEARS
ANNUAL ECG / TTE	ECG / TTE EVERY 5 YEARS



- **Septal myomectomy:** preferable in most cases (especially young patients; septum > 30 mm; other concomitant surgical indication; structural abnormality of mitral valve)
- **Complications:** mortality (1%); complete AV block (2%); LBBB; iatrogenic VSD (< 1%); Ao valve lesion (AR)
- **Alcohol septal ablation:** selective injection of alcohol into perforating septal coronary branches; under ultrasound guidance (with intracoronary contrast); "controlled" infarction targeting the basal ventricular septum at the site of SAM
- **Complications:** mortality (2%); complete AV block (10-20%); RBBB; in-hospital VT (5%); repeat procedures (12%); possible long-term arrhythmic risk

PROGNOSIS: cardiovascular death 1-2 % / year; the majority of patients have a **similar life expectancy to that of the general population**; identify patients with increased risk of sudden death

HCM RISK-SCD (5 years): = $1 - 0.998^{\text{Prognostic index}}$; **consider ICD if 5-year risk ≥ 6%**

- **Prognostic index:** = $[0.15939858 \times \text{maximal wall thickness (mm)}] - [0.00294271 \times \text{maximal wall thickness}^2 \text{ (mm}^2\text{)}] + [0.0259082 \times \text{LA diameter (mm)}] + [0.00446131 \times \text{maximal LVOT gradient (mmHg)}] + [0.4583082 \times \text{familial history SCD}] + [0.82639195 \times \text{NSVT}] + [0.71650361 \times \text{unexplained syncope}] - [0.01799934 \times \text{age (years)}]$

5.9/ DILATED CARDIOMYOPATHY

Ventricular dilatation and systolic dysfunction

Idiopathic in 50% of cases

CLINICAL FEATURES: JVD; lateralized and enlarged apex; S3; S4; AV valve regurgitation

COMPLICATIONS: Heart failure; arrhythmias; conduction disorders; thromboembolism; sudden death

ECG: Sinus tachycardia; arrhythmias; T - ST abnormalities; LVH; poor precordial progression of R wave; conduction disorders

TTE: Spherical LV; thinned walls; dilated chambers; MR (Carpentier I and IIb); limited aortic valve opening; LVOT VTI < 18 cm; ∇ dP/dT; thrombus; diastolic dysfunction; pericardial effusion; PHT

ASSESSMENT: CXR; CBC; Electrolytes; Phosphorus; Calcium; Renal function; LFTs; TSH; CK; ANA; ESR; CRP; Iron assessment; HIV; Urinalysis; Blood glucose; Lipid profile; \pm Lyme antibody titer; \pm Urine metanephrines; \pm BNP

- > **Family screening / Genetic Test:** consider when: **A)** DCM is possibly familial; **B)** DCM with AV block and/or sudden death in the family (LMNA; SCN5A)

SPECIFIC ENTITIES

TACHYCARDIOMYOPATHY: secondary to sustained supraventricular or ventricular tachycardia; recovery of LV function by aggressive rhythm control or rate control within 4 weeks

- > **AF:** BB; Amiodarone x 1 month then cardioversion; Digoxin; RF ablation

ALCOHOLIC CARDIOMYOPATHY: improvement of LVEF with abstinence

- > **Harmful effects of alcohol (heavy drinking):** systolic and/or diastolic dysfunction; HTN; CAD (**decreased risk with low consumption / 1 to 2 standard drinks per day**); stroke; arrhythmia - AF; sudden death; hypertriglyceridemia

OBESITY-RELATED CARDIOMYOPATHY: Secondary to \nearrow cardiac output and myocardial fat infiltration; LV dilatation then LV dysfunction

- > Suspect when BMI > 40 kg/m² (for more than 10 years); Diagnosis of exclusion

CHAGAS DISEASE (TRYPANOSOMIASIS): *Trypanosoma cruzi*; transmission of the parasite by *Triatominae* bugs

- > **Early infection:** Acute myocarditis; \pm meningoencephalitis / skeletal muscle involvement / nerve involvement
 - **Treatment:** Nifurtimox or Benznidazole
 - **Reactivation:** Immunosuppression / HIV / heart transplant
- > **Latent infection:** Mild lymphocytic myocarditis
- > **Chagas cardiomyopathy:** 30% of patients; several years after infection; autoimmune myocarditis (little or no residual parasites); dilatation of chambers; ventricular dysfunction (RV then LV); apical and inferolateral aneurysm; thrombus (apex; RAA); embolism; ventricular arrhythmia; blocks; cardiac dysautonomia

5.10/ RESTRICTIVE CARDIOMYOPATHY

High filling pressure secondary to **rigid myocardium** due to **myocardial or endomyocardial fibrosis or following infiltration of the myocardium by a substance**

PRESENTATION: dyspnea; weakness; edema / anasarca; AF

CLINICAL FEATURES: JVD; Kussmaul's sign; S3; S4; palpable apex (contrary to constriction); AV valve regurgitation; hepatomegaly; ascites; peripheral edema

ECG: **low voltage**; conduction disorders; poor precordial progression of R wave; AF

TTE: **bi-atrial dilatation**; **normal or decreased ventricular volume**; normal or slightly increased wall thickness; sparkling myocardium; thickening of valves / interatrial septum; diastolic dysfunction with restrictive pattern; effusion

	CONSTRICTION	RESTRICTION
Y descent	Prominent	Prominent
Pulsus paradoxus	Sometimes present (1/3)	Absent
Palpable apex	No	Yes
Pericardial knock	Present	Absent
LV filling pressure > 25 mmHg	Rare	Frequent
Square root sign	Present	Present
LVEDP - RVEDP (equalization of diastolic pressures)	< 5 mmHg	> 5 mmHg
RVEDP / RVSP (pulse pressure)	> 0.33	< 0.33
sPAP	< 50 mmHg	> 50 mmHg
Ventricular interdependence (discordant respiratory variations of RV and LV pressures)	Present (pressure discordance)	Absent (pressure concordance)
Diastolic pattern	Restrictive	Restrictive
Respiratory variations of transvalvular flow	Exaggerated • M valve: > 25 % variation • T valve: > 40 % variation	Normal • M valve: about 5% variation
Mitral septal annulus E'	> 8 cm/s	< 8 cm/s
Hepatic veins: ↗ diastolic reversal	Expiratory	Inspiratoire
Ventricular wall thickness	Normal	± Increased
Pericardial thickness	± Increased	Normal
Atrial dimensions	± LA dilatation	Bi-atrial dilatation ++
Abnormal respiratory movement of the septum	Present	Absent
BNP	Often normal	Increased

BIOPSY: Rule out infiltration (amyloidosis; sarcoidosis; Gaucher; Hurler's)

MANAGEMENT

- > Treatment of underlying cause
- > Control of blood volume is difficult (hypotension if ↘ preload)
- > Caution with BB and CCB: cardiac output depends on HR (**fixed stroke volume** due to poor filling)

SPECIFIC ENTITIES

SCLERODERMA: microvascular spasm with ischemia and necrosis / fibrosis

HEMOCHROMATOSIS: tissue iron deposits (heart; liver; gonads; pancreas; skin)

- Autosomal recessive; HFE gene mutation
- **Secondary iron overload:** repeated transfusions; ineffective erythropoiesis
- **Pentad:** heart failure; cirrhosis; impotence; DM; arthritis
- **Cardiac involvement:** diastolic dysfunction - RCM (possibly followed by systolic dysfunction); LV dilatation - DCM; conduction disorders
- **Assessment:** ↗ ferritin (> 200 µg/L in premenopausal women; > 300 µg/L in men or postmenopausal women); ↗ transferrin saturation (> 50% in women and > 60% in men)
- **MRI:** ↘ relaxation time on T2* (< 20 ms)
- **TREATMENT:** Phlebotomies; Chelator (Deferoxamine)

FABRY DISEASE: X-linked; α-galactosidase A deficiency; accumulation of glycosphingolipids in lysosomes

- **Diagnosis:** ↗ urinary globotriaosylceramide; skin biopsy
- Variable degree of enzyme deficiency: **A) Total deficiency:** neuropathies; renal / skin / cardiac involvement; stroke; **B) Partial deficiency:** isolated cardiac involvement is possible
- **Cardiac involvement:** LVH mimicking HCM; Diastolic dysfunction - RCM; angina / myocardial infarction (endothelial infiltration); HTN; MVP
- **Management:** enzyme replacement therapy

SARCOIDOSIS: multisystem noncaseating granulomas (particularly in lungs / reticulo-endothelial system / skin)

- **Cardiac involvement:** infiltration of cardiac conduction tissue and myocardium (IV septum; LV free wall); blocks; ventricular arrhythmias; RCM; systolic LV dysfunction; LV dilatation; LV aneurysm; RWMA not corresponding to coronary anatomy; pericarditis; valvular heart disease; cor pulmonale (pulmonary fibrosis)
- **Biopsy:** often falsely negative
- **MRI:** late gadolinium enhancement reflecting intramural or subepicardial fibrosis (often anteroseptal or inferolateral)
- **PET-FDG:** demonstrates patchy zones of fibrosis and/or inflammation
- **Management:** Corticosteroids; Plaquenil; Methotrexate; Cyclophosphamide; ICD; Transplant (risk of recurrence)

ENDOMYOCARDIAL FIBROSIS (DAVIES DISEASE): Tropical regions; ± eosinophilia; fibrosis / thrombus / endocardial obliteration (obliteration of apex; papillary muscle fibrosis; AV valve regurgitation); bi-atrial dilatation; diastolic dysfunction with restrictive pattern

LOEFFLER ENDOCARDITIS (HYPEREOSINOPHILIC SYNDROME): Eosinophilia > 1 500 cells/µL with multisystem involvement (lung; CNS; GI; skin)

- **Cardiac involvement:** myocarditis followed by replacement of the myocardium by thrombus then formation of endomyocardial fibrosis; fibrosis / thrombus / endocardial obliteration (apex; posterior mitral leaflet; posterobasal wall); RCM; AV valve regurgitation; embolism
- **Management:** anticoagulation; Corticosteroids; Hydroxyurea; Interferon; endocardectomy; valve replacement / repair

CARCINOID SYNDROME: Gastrointestinal tract (small bowel) or bronchial tumor; release of serotonin by the tumor and liver metastases; ↗ urinary 5-HIAA

- **Symptoms:** skin flushing; diarrhea; bronchospasm; hypotension
- **Cardiac involvement:** Fibrous endomyocardial plaques in right heart chambers; tricuspid and pulmonary valve disease with thickening / retraction / rigidity of leaflets (TR and PR due to malcoaptation; ± TS; ± PS); right ventricular dilatation and dysfunction
 - **Involvement of left chambers in the presence of R→L shunt or lung metastases**
- **Management:** Somatostatin analogs; embolization of liver metastases; TVR if severe symptoms and/or dilatation – progressive RV dysfunction (despite adequate control of the cancer)

5.11/ CARDIAC AMYLOIDOSIS

Interstitial infiltration of a protein demonstrating apple-green birefringence when stained with Congo Red

PRIMARY AMYLOIDOSIS (AMYLOIDOSIS AL)

Plasma cell dyscrasia (plasma cell clone); tissue deposits of a portion of **immunoglobulin light chains**

CARDIAC INVOLVEMENT (50% OF PATIENTS): median survival = 15 months; LVH; RCM; progressive LV dysfunction; ischemia (microvascular infiltration); conduction disorders; atrial disease; sudden death (pulseless electrical activity)

SYSTEMIC INVOLVEMENT: OH; peripheral / autonomic neuropathy; carpal tunnel; periorbital purpura; ecchymoses; macroglossia; RUQ pain; onychodystrophy; renal failure / nephrotic syndrome

CLINICAL FEATURES: hypotension / OH; JVD; Prominent X and Y waves; Kussmaul; S4 rarely present (atrial disease); pleural effusions; hepatomegaly; anasarca

ECG: **microvoltage (despite LVH on TTE)**; AF; pseudo-infarction; blocks

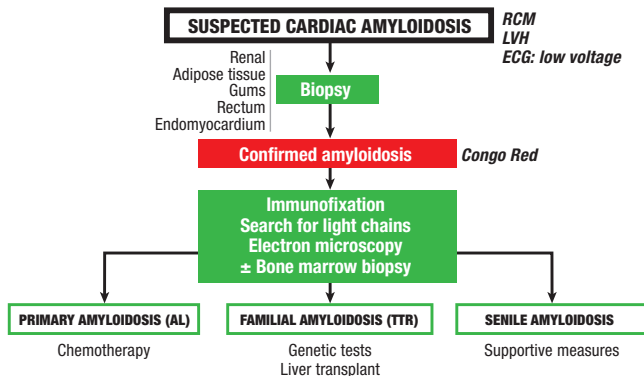
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TTE: thickened walls; small ventricular chamber; dynamic LVOT obstruction; valvular / interatrial septum infiltration; sparkling myocardium; diastolic dysfunction; possible systolic dysfunction; pericardial effusion; bi-atrial dilatation

CARDIAC MRI: rapid accumulation of contrast in myocardium (**rapid wash-out from blood**); circumferential subendocardial or patchy transmural late gadolinium enhancement; atrial left gadolinium enhancement

DIAGNOSIS: biopsy of abdominal adipose tissue (positive in > 70% of cases) or gums or salivary glands or kidney or rectum or endomyocardial tissue

- If Congo Red positive → **Distinguish primary (AL) from familial (TTR) amyloidosis**
 - Serum and urinary immunofixation (± SPEP and UPEP)
 - Electron microscopy immunohistochemistry techniques
 - Abnormal kappa / lambda light chain ratio
- Bone marrow biopsy: % plasma cells; rule out MM and Waldenström



MANAGEMENT

- > Cautious use of Lasix; **particular caution with vasodilators and Digoxin**
- > Anticoagulation in the presence of AF or atrial disease (A wave < 20 cm/s)
- > **Anti-plasma cell chemotherapy:** Melphalan / Dexamethasone or Cyclophosphamide / Thalidomide / Dexamethasone; High-dose chemotherapy combined with autologous bone marrow transplantation as required

FAMILIAL AMYLOIDOSIS**Mutant transthyretin protein (TTR) (in the majority of cases)**

Autosomal dominant; most patients develop clinical features after the age of 40 years

PRESENTATION: various degrees of cardiac / conduction tissue / peripheral nerve / renal involvement

TREATMENT: liver transplant (mutant TTR produced by the liver)

SENILE CARDIAC AMYLOIDOSIS

Non-mutant transthyretin protein (TTR)

Rare extracardiac involvement

SUSPECT: in an elderly patient with heart failure + LV wall thickening + normal chamber dimensions; frequent blocks; AF

DIAGNOSIS: endomyocardial biopsy

Median survival: 7.5 years

5.12/ ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA (ARVD)

RV dysfunction (regional or global) secondary to infiltration of the myocardium by fibrous / adipose tissue

- > **Triangle of dysplasia:** lesion of the RV inflow tract, RV outflow tract and apex of the RV
- > LV is sometimes involved; can mimic DCM

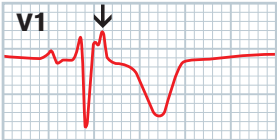
AUTOSOMAL DOMINANT: majority of cases; desmosome protein gene

- > **Autosomal recessive: Naxos syndrome** (plakoglobin; woolly hair; palmoplantar keratoderma); **Carvajal syndrome** (desmoplakin; palmoplantar keratoderma; predominant LV involvement)

4 PHASES

1. Asymptomatic
2. Arrhythmic (palpitations; syncope; VT – sudden death)
3. Right heart failure
4. Biventricular failure / DCM

DIAGNOSIS: requires the presence of several criteria

MAJOR CRITERIA	MINOR CRITERIA
01. Structural lesion	
TTE a) RV: regional akinesia or dyskinesia or aneurysm + b) PLAX RVOT ≥ 32 mm or PSAX RVOT ≥ 36 mm (end-diastole) or FAC $\leq 33\%$ MRI a) RV: regional akinesia or dyskinesia or dyssynchrony + b) RV end-diastolic volume ≥ 110 mL/m ² (M) or ≥ 100 mL/m ² (F) or RVEF $\leq 40\%$ Angiography • RV: regional akinesia or dyskinesia or aneurysm	TTE a) RV: regional akinesia or dyskinesia + b) PLAX RVOT 29 to 32 mm or PSAX RVOT 32 to 36 mm (end-diastole) or FAC 33% to 40% MRI a) RV: regional akinesia or dyskinesia or dyssynchrony + b) RV end-diastolic volume 100 to 110 mL/m ² (M) or 90 to 100 mL/m ² (F) or RVEF 40 to 45%
02. Tissue characterization (biopsy)	
Residual myocytes < 60% with fibrous replacement of RV free wall with or without fat replacement	Residual myocytes 60 - 75% with fibrous replacement of the RV free wall with or without fat replacement
03. Repolarization abnormalities	
T wave inversion in V1-V2-V3 (absence of cRBBB with QRS ≥ 120 ms)	• T wave inversion in V1-V2 (absence of RBBB with QRS ≥ 120 ms) or V4 or V5 or V6 • T wave inversion in V1-V2-V3-V4 with cRBBB
04. Depolarization / conduction abnormalities	
Epsilon wave in V1-V2-V3 (low amplitude signal between the end of the QRS and the start of the T wave) 	• Late potentials (SAECG): $\geq 1/3$ positive parameters (absence of QRS ≥ 110 ms on basic ECG) a) Filtered QRS ≥ 114 ms b) Terminal QRS (< 40 μ V) ≥ 38 ms c) RMS (Root mean square) of terminal 40 ms ≤ 20 μ V • QRS: S nadir to the end of the QRS ≥ 55 ms in V1 - V2-V3 (absence of cRBBB)
05. Arrhythmias	
NSVT or VT with LBBB morphology with superior axis (negative QRS in II - III - aVF and positive QRS in aVL)	• NSVT or VT of RVOT, LBBB morphology with inferior axis (positive QRS in II - III - aVF and negative QRS in aVL) or unknown axis • > 500 PVCs per 24 h
06. Family history	
• 1st degree relative meeting the criteria • 1st degree relative with histologically confirmed diagnosis • Pathogenic mutation	• History of ARVD in 1 st degree relative (but impossible to verify criteria) • Sudden death < 35 years in a 1 st degree relative with suspected ARVD • Confirmed ARVD (histology or criteria) in a 2 nd degree relative
• Definitive diagnosis: 2 major or 1 major + 2 minor or 4 minor (different categories) • Borderline diagnosis: 1 major + 1 minor or 3 minor (different categories) • Possible diagnosis: 1 major or 2 minor (different categories)	

Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia. Proposed Modification of the Task Force Criteria. *Circulation*. 2010;121: 1533-1541.

OTHER ELEMENTS TO LOOK FOR: **A)** \nearrow QRS duration > 100 ms in V1 (delayed activation of RV; RBBB); **B)** Multiple RV scars on electrophysiological voltage mapping; **C)** Fat infiltration of RV on MRI (marked inter-observer variability)

DDX: **A)** DCM; **B)** Uhl's anomaly (zones in RV with absence of myocardium; endocardium and epicardium are continuous); **C)** Idiopathic RVOT VT (ECG / SAECG / TTE all normal); **D)** Myocarditis; **E)** Sarcoidosis

MANAGEMENT

- > Avoid competitive sports or symptomatic exertion; Screening in 1st degree relatives
- > Treatment of heart failure: ACE inhibitors; BB; Heart transplantation PRN
- > ICD:
 - a) **Secondary prevention:** documented sustained VF / VT
 - b) **Primary prevention:** consider ICD \rightarrow unexplained syncope; frequent NSVT; family history of premature sudden death; extensive disease (extensive RV involvement; LV involvement); marked QRS prolongation; VT induction during EPS
 - c) **Frequent shocks:** Sotalol; Amiodarone; VT ablation

5.13/ ISOLATED LEFT VENTRICULAR NONCOMPACTION

Failure of endomyocardial compaction during embryogenesis

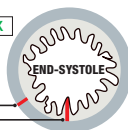
Prominent trabeculations with deep intertrabecular crypts

Isolated (autosomal dominant or sporadic) vs **associated with congenital heart disease** (Ebstein; RVOT or LVOT obstruction; complex heart disease)

PRESENTATION: heart failure; arrhythmia; sudden death; embolism

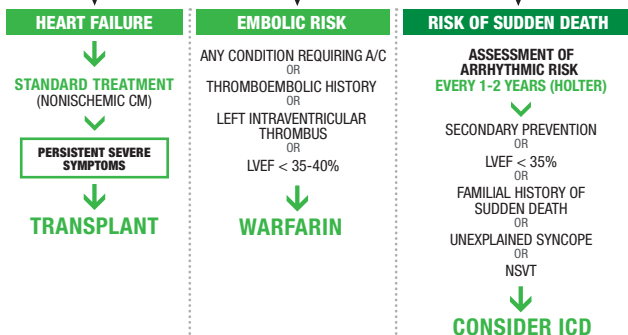
TTE (\pm CONTRAST): thin epicardial layer with thick non-compacted endomyocardial layer (predominantly apical and middle portions of inferior and lateral walls); **intertrabecular crypts continuous with the intraventricular cavity** (blood flow on color Doppler); RWMA; LV dysfunction; thrombus; abnormal papillary muscle

PSAX



Non-compacted endomyocardium
Compact myocardium > 2

LV NONCOMPACTION



MRI: non-compacted endomyocardium / compacted myocardium ratio > **2.3 in diastole**



MANAGEMENT: screening of 1st degree relatives (TTE); avoid competitive sports

5.14/ TAKOTSUBO CARDIOMYOPATHY (STRESS CARDIOMYOPATHY)

Transient systolic dysfunction involving the apex (\pm midventricular walls) in the absence of any significant CAD; often following an intense emotional or physical stress

- > Secondary to catecholamine surge
- > Postmenopausal women in > 90% of cases
- > **Variants:** isolated midventricular lesion or reverse Takotsubo (basal akinesia)

PRESENTATION: Retrosternal chest pain; ST elevation on ECG or diffuse T wave inversion (with \uparrow QT); \uparrow troponin (limited); negative coronary angiography

- > **Complications:** hemodynamic instability (LVOT obstruction \pm SAM secondary to basal hyperdynamism in 15% of cases); heart failure; arrhythmias; thromboembolism; MR (SAM)
- > **Complete recovery of LV function in 1 to 3 months; good prognosis**

CARDIAC MRI: myocardial edema; apical akinesia; absence of fibrosis - necrosis

DDX: Intracranial hemorrhage or SAH (often **basal and mid-ventricular akinesia**); major stroke; Pheochromocytoma (rule out if recurrence); Vasospasm; Cocaine; Amphetamines; Myocarditis

MANAGEMENT

- > Carvedilol (alpha / beta blocker)
- > ACE inhibitor (stop after recovery)
- > TTE at 1 and 3 months (consider alternative diagnosis if LV dysfunction persists)
- > **Anticoagulation: A)** Anticoagulant therapy if LV thrombi; **B)** Prophylactic anticoagulation may be considered to prevent LV thrombi (class IIb recommendation)
- > **Hypotension / Shock:**
 - **Severe systolic dysfunction without LVOT obstruction:** Amines (cautiously); IABP as required
 - **LVOT obstruction:** BB (avoid amines); Volume (in absence of overload); Phenylephrine (cautiously)

5.15/ MYOCARDITIS

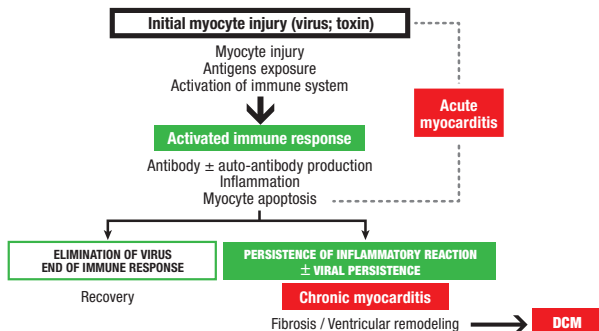
Inflammation of the myocardium

DALLAS CRITERIA: presence of **inflammatory cells** (lymphocytes) \pm **myocyte necrosis** on biopsy; poor sensitivity (often falsely negative)

ETIOLOGIES

- > **Virus:** Coxsackievirus; echovirus; adenovirus; parvovirus B19; CMV; HSV6; HIV; influenza; HCV; EBV
- > **Bacteria / Spirochete:** TB; *Chlamydia pneumoniae*; *Streptococcus*; *Mycoplasma pneumoniae*; *Treponema pallidum*; *Clostridium*; Diphtheria; Whipple; Lyme
- > **Fungi:** *Aspergillus*; *Candida*; *Coccidioides*; *Cryptococcus*; *Histoplasma*
- > **Parasites:** Chagas; Schistosomiasis; Echinococcosis
- > **Toxins:** Anthracyclines; Cocaine; 5-FU; phenytoin; cyclophosphamide; arsenic; iron; radiotherapy; alcohol; amphetamines; carbon monoxide; heatstroke; hypothermia; insect / snake bite
- > **Hypersensitivity:** clozapine; sulfonamides; cephalosporins; tetracyclines; PNC; tricyclic antidepressants; allopurinol; dobutamine; diuretics
- > **Autoimmune:** giant cell myocarditis; Churg-Strauss; Sjögren; inflammatory bowel disease; celiac disease; sarcoidosis; SLE; Takayasu arteritis; Wegener; dermatomyositis; Kawasaki; RA; scleroderma; thyrotoxicosis

PATHOPHYSIOLOGY



PRESENTATION

Compatible symptoms: Acute retrosternal chest pain mimicking myocardial infarction or pericarditis; heart failure; palpitations; syncope; sudden death; cardiogenic shock; viral prodromes; fever

+ ≥ 1 DIAGNOSTIC CRITERION

ECG: AV block (Lyme; giant cell; sarcoidosis); branch block; ST-T abnormalities; PVCs; VT - VF; AF; sinus arrest; low voltage; Q waves	Myo-cardio-cytolysis: elevated troponins	Structural / functional abnormalities (TTE): RWMA; systolic dysfunction; ventricular dilatation; wall thickening; effusion; thrombus	MRI (Lake Louise criteria) <ul style="list-style-type: none"> • Early gadolinium enhancement on T1 indicating inflammation (myocardium vs skeletal muscle enhancement ratio > 4.0) • Late gadolinium enhancement indicating fibrosis (intramural or subepicardial; often anteroseptal or inferolateral) • ↑ T2 signal intensity indicating edema (myocardium vs skeletal muscle signal ratio > 2.0)
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- **Fulminant lymphocytic myocarditis:** < 2 weeks after a viral infection; hemodynamic instability; diffuse LV dysfunction (rarely dilatation); wall thickening (edema); good prognosis with support
- **Giant cell myocarditis:** heart failure (evolving over several weeks to several months); blocks; ventricular arrhythmias; deterioration despite treatment; often underlying autoimmune disease (thymoma; Crohn); median survival < 6 months; Treatment: immunosuppression; transplant
- **Acute lymphocytic myocarditis:** may mimic acute MI (with negative coronary angiography) or may present with progressive LV dysfunction / dilatation or fulminant myocarditis; can progress to DCM
- **Eosinophilic myocarditis:** Hypersensitivity or Loeffler endocarditis or acute necrotizing eosinophilic myocarditis
 - **Hypersensitivity:** drug reaction; rash; fever; multiple organ dysfunction; eosinophilia; Myocarditis; Treatment with corticosteroids
 - **Acute necrotizing eosinophilic myocarditis:** rare; poor prognosis
- **Chronic active myocarditis:** insidious; LV systolic dysfunction (sometimes diastolic with restrictive pattern); ± viral persistence

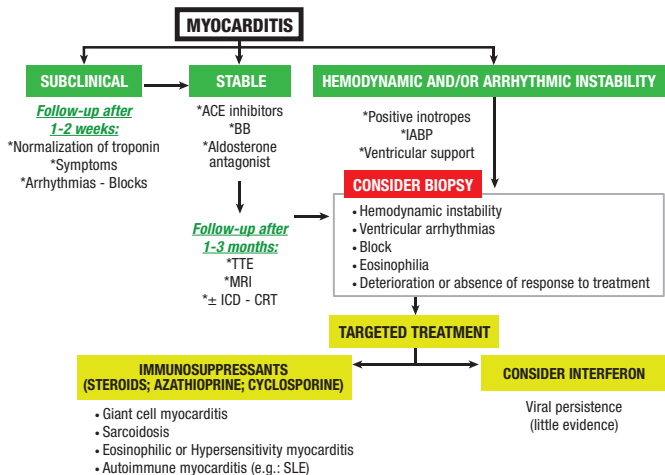
DEFINITIVE DIAGNOSIS: myocarditis with **histological and/or immunohistological proof** on biopsy



CONSEQUENCES: viral persistence and/or persistent activation of immune system; chronic myocarditis; myocyte necrosis / fibrosis; remodeling; DCM; arrhythmia - sudden death

MANAGEMENT

- > Avoid strenuous exertion / competitive sports for ≥ 6 months



5.16/ INDICATIONS FOR ENDOMYOCARDIAL BIOPSY

1. Heart failure for < 2 weeks with hemodynamic compromise (fulminant lymphocytic myocarditis; necrotizing eosinophilic myocarditis; giant cell myocarditis) (I;B)	+
2. Heart failure for 2 weeks to 3 months with LV dilatation and ventricular arrhythmias or AV block (2 nd or 3 rd degree) or absence of response to treatment (1-2 weeks) (giant cell myocarditis or eosinophilic myocarditis) (I;B)	
3. Heart failure for > 3 months with LV dilatation and ventricular arrhythmias or AV block (2 nd or 3 rd degree) or absence of response to treatment (1-2 weeks) (sarcoidosis or Chagas) (IIa;C)	
4. Heart failure with dilated cardiomyopathy and suspicion of allergic reaction and/or eosinophilia (eosinophilic myocarditis) (IIa; C)	
5. Heart failure with suspicion of anthracycline cardiomyopathy (detect at an early stage of cardiotoxicity) (IIa; C)	
6. Heart failure with unexplained RCM (IIa; C)	
7. Suspected cardiac tumor (with the exception of myxoma), when noninvasive method is inconclusive (IIa; C)	

COMPLICATIONS OF BIOPSY: 3%; venous access (arterial puncture; pneumothorax; bleeding); arrhythmia; blocks - RBBB; valve injury; cardiac perforation; tamponade; death; stroke (LV biopsy)

5.17/ CARDIAC TUMORS

METASTASIS

Direct extension; hematogenous; extension via IVC (Hypernephroma; intravenous leiomyomatosis)

Lung; Breast; Lymphoma; Leukemia; Kaposi; Esophagus; Melanoma; Stomach; Mesothelioma; Thyroid; Renal; Extracardiac sarcoma

PRIMARY TUMORS

75 % benign



SYSTEMIC FEATURES: fever; malaise; weight loss; anemia

EMBOLIC PHENOMENA: tumor embolism or thromboembolism

CARDIAC SIGNS: depending on the site of the tumor; blocks - arrhythmia; valve obstruction or regurgitation; SVC syndrome; coronary artery compression; hemorrhagic pericardial effusion (angiosarcoma; lymphoma); heart failure

DIAGNOSIS: TTE; TEE; CT scan or MRI (**mass visible if > 1 cm**); biopsy; metastatic work-up of malignant tumors; PET scan

- > **MRI:** distinction between tumor and thrombus (according to gadolinium enhancement); tissue characterization

MYXOMA

Pedunculated mass with stalk attached to the endocardium (often interatrial septum)

LA (80%); RA (10%); > 90% are solitary

PRESENTATION: Constitutional symptoms; embolisms (tumor fragment or thrombus); valve obstruction (can vary according to the position; look for tumor "plop"); extracardiac metastases

Recurrence in 3% of cases; TTE follow-up for life

Family screening (5 to 10% are familial)

- > **Carney complex:** autosomal dominant; multiple intracardiac and extracardiac myxomas; high recurrence rate; cutaneous lentiginosities; other tumors (testicular; pituitary; thyroid)

TREATMENT: surgical resection

PAPILLARY FIBROELASTOMA

On **valvular endocardium** (80-90%); aortic valve (40%; aortic side); mitral valve (30%; ventricular side); rarely endocardium of LA or LV; solitary (90%)

Friable lesion measuring about 1 cm; resembles a sea anemone; adherent thrombus; 45% have a stalk (1-3 mm)

COMPLICATIONS: thromboembolism

TREATMENT: surgical resection (especially if embolism or mobile or > 1 cm)

LIPOMA

Especially subendocardial (also subepicardial or myocardial)

Predominantly solitary (multiple in the case of tuberous sclerosis)

MRI: fatty mass

COMPLICATIONS: obstruction; pericardial effusion; block; arrhythmias

TREATMENT: surgical resection when symptomatic

LIPOMATOUS HYPERTROPHY OF INTERATRIAL SEPTUM

Excessive fat accumulation in the interatrial septum

Thickening spares the fossa ovale; dumbbell appearance

Associated with obesity and age > 70 years

COMPLICATIONS: Blocks; arrhythmias; SVC obstruction (rare)

RHABDOMYOMA

Children; **associated with tuberous sclerosis** (autosomal dominant; epilepsy; skin lesions; hamartomas)

Ventricles > atria; **multiple lesions; spontaneous regression**

FIBROMA

Children (sometimes adults)

Solitary intramural mass; interventricular septum or LV free wall

TREATMENT: Surgical resection when symptomatic (arrhythmia; blocks; obstruction)

HEMANGIOMA / LYMPHANGIOMA

Intrachamber (ventricle > atrium) / intramural / epicardium / pericardium

Coronary angiography sometimes demonstrates the tumor blood supply

PRESENTATION: asymptomatic; palpitations; heart failure; pericardial effusion; obstruction; embolism; AV block

TREATMENT: echocardiographic follow-up (may increase in size or disappear); surgical resection when symptomatic

MALIGNANT TUMORS

ANGIOSARCOMA

- **RA in 90% of cases** (intramural mass protruding into the chamber)
- Frequent pericardial involvement
- Metastasis at presentation in 70-80% of cases (lung; liver; CNS; bone)
- Mean survival: 10 months
- **Treatment:** Surgery; Radiotherapy; Chemotherapy (Doxorubicin); Neoadjuvant chemotherapy (reduce tumor size prior to surgery); IL-12; autologous transplant (with ex vivo resection); transplant; palliative care

RHABDOMYOSARCOMA

- Children - young adults
- Multiple lesions (60%); no predilection for a particular chamber
- Aggressive, invasive tumor; metastases (lungs; lymph nodes)
- Survival < 1 year

LEIOMYOSARCOMA

- > **LA (70-80 %)**; solitary (70%)
- > Rapid growth; metastases; mean survival: 6 months

CARDIAC LYMPHOMA

- > Right heart (70%); solitary (66%)
- > Pericardial effusion (50%)
- > Frequent extracardiac disease at the time of presentation
- > **Treatment:** Anthracycline; Radiotherapy; Rituximab

5.18/ CARDIAC COMPLICATIONS OF CANCER

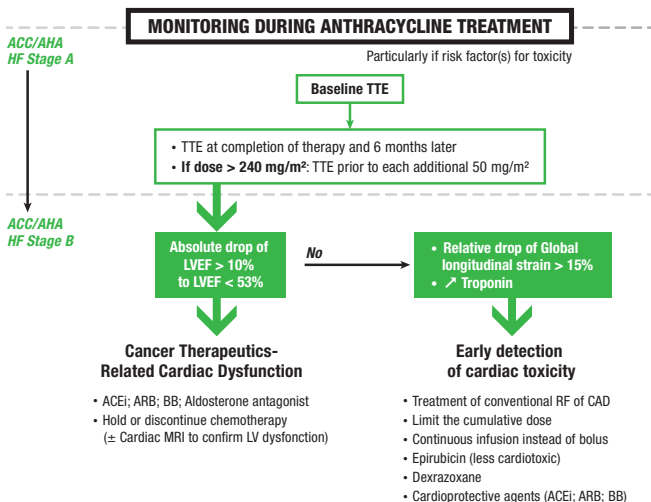
COMPLICATIONS: **A)** Metastases; **B)** Pericardial effusion; **C)** Tamponade; **D)** Constriction (radiotherapy); **E)** SVC obstruction; **F)** Valvular heart disease (metastases; infective endocarditis or non-bacterial thrombotic endocarditis; radiotherapy; obstruction; carcinoid); **G)** CAD (common risk factors; cancer chemotherapy; radiotherapy); **H)** Hyperviscosity (erythrocytosis or thrombocytosis or leukocytosis; \nearrow Ig); **I)** Cardiotoxicity of chemotherapy and radiotherapy

ANTHRACYCLINE TOXICITY: (Doxorubicin; Daunorubicin; Epirubicin; Idarubicin)

> **Acute toxicity:** myocarditis; pericarditis; pericardial effusion; arrhythmia; ventricular dysfunction

> **Chronic toxicity:** type I cardiotoxicity (irreversible, dose-dependant damage) leading to \searrow LVEF / DCM

> **Risk factors for toxicity:** cumulative dose > 350 mg/m²; bolus; females; young; > 65 ans; $+$ risk factors for heart disease; history of heart disease; mediastinal radiotherapy; **Trastuzumab** (TTE every 3 months during treatment) or **Cyclophosphamide** or **Paclitaxel**; baseline LVEF < 55 %



MEDIASTINAL RADIOTHERAPY: fibrosis and calcification of cardiac structures; complications often occur 10-20 years post-exposure; **higher risk with cumulative dose > 30 Gy** +

- > **Complications:** **A)** Accelerated CAD; **B)** Blocks / Conduction system disease; **C)** Valvular heart disease (thickening / fibrosis / calcification; predominant on left-sided valves; regurgitation > stenosis); **D)** Constrictive pericarditis; Pericardial effusion; **E)** Diffuse myocardial fibrosis with diastolic dysfunction / RCM; **F)** Carotid artery disease (Stroke – TIA); **G)** Aortic calcification / Porcelain aorta; **H)** Recurrent pleural effusions
- > **Prevention:** minimize dose to the heart; cardiac shielding; reduction of dose-volume; decreased field; breath-holding; treatment of conventional risk factors of CAD
- > **Monitoring after chest radiation exposure:** TTE 5-10 years after exposure then re-assess every 5 years; consider stress-test for CAD detection

SPECIFIC CARDIAC COMPLICATIONS OF CHEMOTHERAPY

LV DYSFUNCTION: Anthracyclines (type I cardiotoxicity; permanent dose-dependant damage); Trastuzumab (type II cardiotoxicity; reversible damage; TTE every 3 months during therapy); Cyclophosphamide; Ifosfamide; Clofarabine; Docetaxel; Paclitaxel (in combination with Doxorubicin); Bevacizumab; Bortezomib; Dasatinib; Imatinib; Sunitinib

ISCHEMIA / VASOSPASM: Capecitabine; 5-Fluorouracil; Paclitaxel; Docetaxel; Bevacizumab (arterial thromboses); Rituximab; Dasatinib; Erlotinib; Sorafenib; Cisplatin; Carboplatin; Interferon

BRADYCARDIA: Thalidomide; Paclitaxel; Docetaxel

HTN: Cisplatin; Docetaxel; Bevacizumab; Rituximab; Trastuzumab; Dasatinib; Sunitinib; Sorafenib; Cyclosporine; Tacrolimus; MMF; Sirolimus

DEEP VEIN THROMBOSIS: Cisplatin; Thalidomide; Bevacizumab; Rituximab; Lenalidomide; Erlotinib; Sorafenib

↗ **QT:** Anthracyclines; Vorinostat; Arsenic trioxide; Dasatinib; Lapatinib; Nilotinib; Sunitinib; Lenalidomide; 5-fluorouracil; Cyclophosphamide; Trastuzumab

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Arrhythmias

06

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6.1/ PHYSIOLOGY

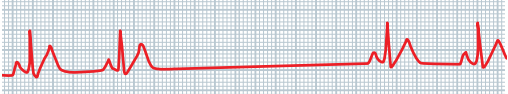
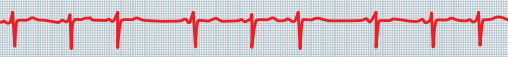
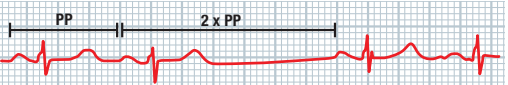
MYOCARDIAL CELLS / HIS / PURKINJE	SINOATRIAL NODE / AV NODE
<p>-90 mV</p> <p>Na+</p> <p>Ca²⁺</p> <p>K+</p>	<p>-40 mV</p> <p>Na(lf)</p> <p>Ca-T</p> <p>Ca-L</p> <p>K+</p> <p>Inactivated rapid sodium channels (higher resting potential)</p>
<ul style="list-style-type: none"> • PHASE 4 (resting potential): -90 mV (extracellular Na⁺; intracellular K⁺) • PHASE 0 (action potential): brief opening of rapid sodium channels (Na⁺ influx) • PHASE 1: inactivation of sodium channels and K⁺ efflux • PHASE 2 (plateau): equilibrium between K⁺ efflux and Ca²⁺ influx via slow calcium channels • PHASE 3 (rapid repolarization): K⁺ efflux 	<ul style="list-style-type: none"> • PHASE 4 (rest): spontaneous depolarization → slow sodium influx via If sodium channel ➢ Intrinsic automaticity: > 60 bpm (SA node) and 40-60 bpm (AV node) • PHASE 0 (action potential): opening of slow calcium channels (Ca²⁺ influx) • PHASE 3 (repolarization): inactivation of calcium channels and potassium efflux

ARRHYTHMIC MECHANISMS

- 1) **ABNORMAL AUTOMATICITY:** ↗ phase 4 diastolic depolarization
- 2) **REENTRY:** two conduction pathways with different conduction velocities and refractory periods; requires one-directional conduction block in one of the pathways of the circuit
- 3) **TRIGGERED ACTIVITY:** abnormality during repolarization
 - **Early afterdepolarization:** Torsade de pointes
 - **Delayed afterdepolarization:** Digoxin poisoning; idiopathic VT; catecholaminergic polymorphic VT

6.2/ BRADYARRHYTHMIAS

SINOATRIAL NODE

Sinus bradycardia	<ul style="list-style-type: none"> • HR < 60 bpm; normal morphology of P wave • Etiologies: benign; vagal hypertonia; athletes; sick sinus syndrome (SSS); drugs (BB; CCB; Digoxin; Ivabradine; Clonidine; Propafenone; Amiodarone); post-cardiac surgery; ischemia / myocardial infarction; myocarditis; infiltrative cardiomyopathy; Lyme disease; coronary angiography; meningitis; intracranial hypertension; stroke; hypoxia; hypothyroidism; hypothermia; Gram-negative bacillus sepsis; cervical / mediastinal tumor; OSAHS; familial SSS (SCN5A mutation); Chagas, ... • Management: observation; Atropine 0.5 mg; PPM if symptomatic
Sinus arrest / Sinus pause	<ul style="list-style-type: none"> • Sudden absence of sinus P wave; the duration of the pause is not a multiple of the intrinsic P–P interval <ul style="list-style-type: none"> ➢ Ventricular asystole if absence of escape rhythm by latent pacemakers  <ul style="list-style-type: none"> • Etiologies: ➤ Sinus bradycardia • Tachy-bradycardia syndrome: supraventricular tachyarrhythmia alternating with sinus bradycardia; ± sinus pause following conversion of the tachyarrhythmia; associated with sick sinus syndrome (SSS) • Management: PPM if symptomatic
Sinoatrial block (SA exit block)	<ul style="list-style-type: none"> • Sinoatrial block, 2nd degree - Mobitz I: progressive reduction of P-P interval then absence of P wave; duration of the pause < twice the P-P interval; group beating  <ul style="list-style-type: none"> • Sinoatrial block, 2nd degree - Mobitz II: sudden absence of P wave; the duration of the pause is a multiple of the intrinsic P–P interval 
Wandering atrial pacemaker	<ul style="list-style-type: none"> • Passive and gradual shift from a dominant pacemaker focus of the sinoatrial node to a latent atrial pacemaker; a single pacemaker controls rhythm at any one time; possible shift of control back to the sinoatrial node • Mechanism: vigorous vagal tone (benign phenomenon)
Chronotropic incompetence	<ul style="list-style-type: none"> • Inability to achieve > 80% HRmax predicted during a stress test (in the presence of sufficient exercise) <ul style="list-style-type: none"> ➢ Chronotropic index: observed HR reserve (HRmax on stress test - resting HR) / (HRmax predicted for age - resting HR); chronotropic incompetence if < 80 % • Consequences: exercise intolerance; factor of poor prognosis

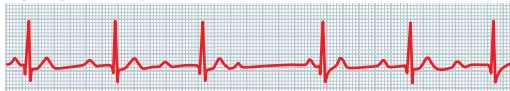
AV CONDUCTION: AV NODE / HIS-PURKINJE SYSTEM

First degree AV block

- **PR > 200 ms** in sinus rhythm
- **Narrow QRS**: delayed AV node conduction (↗ AH)
- **Wide QRS**: delayed AV node conduction (↗ AH) or His-Purkinje conduction (↗ HV)
 - **Bifascicular block (RBBB + LAHB or RBBB + LPHB or LBBB)**: consider a lesion of the third branch in the presence of prolonged PR

2nd degree AV block, Mobitz I (Wenckebach)

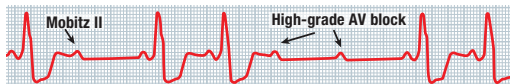
- **Progressive prolongation of the PR interval (with progressive shortening of the RR interval)** until a P wave is blocked; the RR interval including the non-conducted P wave is **less than twice the R-R interval of the previous cycle**; group beating



- **Prognosis**: benign (lesion involving the AV node in the majority of cases)
- **Treatment**: observation if asymptomatic

2nd degree AV block, Mobitz II

- **P wave suddenly blocked** without any previous prolongation of the PR interval; the RR interval at the time of the non-conducted P wave = **twice the PP interval**

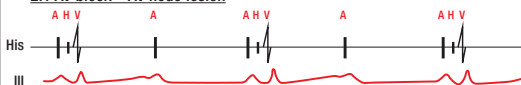


- **Prognosis**: infranodal lesion (His-Purkinje system) in the majority of cases with **high risk of progression to complete AV block**
- **Treatment**: indication for PPM

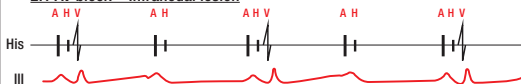
2:1 AV block

- **P:QRS ratio = 2:1**
- **Suggests AV node lesion (benign): A)** Wenckebach on another ECG; **B)** ↗ PR interval (but narrow QRS); **C)** Improvement of the block with exercise or atropine; **D)** Deterioration of the block with carotid sinus massage
- **Suggests infra-nodal lesion (requires PPM): A)** Wide QRS (underlying intraventricular conduction disorder); **B)** Deterioration of the block with exercise or atropine; **C)** Improvement of the block with carotid sinus massage (↗ PP interval → ↗ His-Purkinje system recovery time)

2:1 AV block – AV node lesion



2:1 AV block – Infranodal lesion



High-grade AV block

- **≥ 2 successive P waves blocked** in sinus rhythm

Complete AV block (3rd degree)

- **Absence of AV conduction**
- **Intranodal block:** junctional escape rhythm; narrow QRS; HR 40–60 bpm
- **Infranhisian block:** ventricular escape rhythm (unreliable and unstable); wide QRS; HR 15–40 bpm



- **Etiologies:** degenerative; drugs; congenital; ischemia - MI; vagal hypertonia; surgery; calcified AS; progressive familial heart block (Lenègre's disease; SCN5A or TRPM4 mutation); electrolyte disorders; myocarditis; endocarditis; tumor; Chagas; Lyme disease; rheumatoid nodule; AVR; TAVI; hypothyroidism; polymyositis; dilated cardiomyopathy (lamin A/C); infiltrative cardiomyopathy (amyloidosis; sarcoidosis; scleroderma); muscular dystrophy...
- **Treatment:** Rule out a reversible cause; PPM

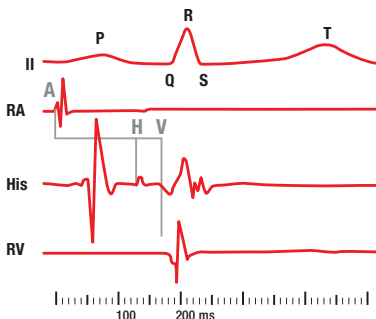
ELECTROPHYSIOLOGICAL STUDY OF CONDUCTION TISSUE

INDICATION: in the presence of a strong suspicion of significant and symptomatic bradyarrhythmia, but in the absence of a clearly documented abnormality

SNRT: Sinus node recovery time

- Continuous rapid atrial stimulation (30 s) then stopped
- **SNRT:** interval between last paced beat and the first sinus return beat
- **CSNRT (corrected SNRT):** = SNRT - CL in sinus rhythm
- **> Normal CSNRT:** < 525 ms
- Low sensitivity (65%) but high specificity (95%)

AV conduction



Intervals measured

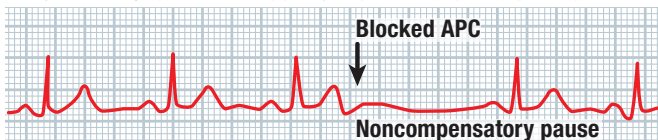
- **AH:** AV node conduction; normal 55–125 ms
- **His conduction time:** normal < 25 ms
- **HV:** infra-His conduction time; normal: 35–55 ms
- **> HV > 100 ms:** possible risk of complete AV block
- **> Short HV:** A) Ventricular pre-excitation; B) PVC or idioventricular rhythm isorhythmic with SR

6.3/ SUPRAVENTRICULAR TACHYARRHYTHMIAS

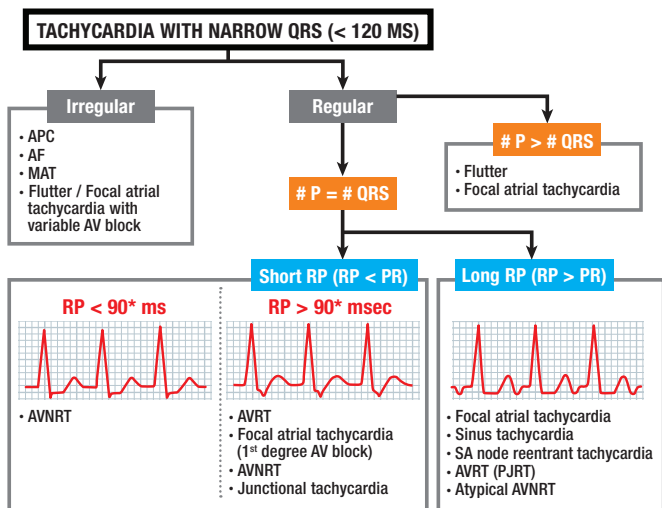
ATRIAL PREMATURE COMPLEXES

ATRIAL PREMATURE COMPLEXES (APC): premature P wave in the cardiac cycle; arises from an atrial focus outside of the sinoatrial node; different morphology from that of the sinoatrial node; sometimes situated in the T wave (look for abnormal morphology of the T wave)

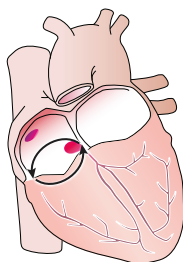
- > **Modifiers:** Couplets; Bigeminy; Trigeminy; Salvo
- > **Noncompensatory pause:** the APC depolarizes and **resets** the sinoatrial node; the interval between the two P waves before and after the APC **< twice the intrinsic PP interval** +
- > **Compensatory pause:** failure of the APC to depolarize the sinoatrial node; the interval between the two P waves before and after the APC = **twice the intrinsic PP interval**
- > **Blocked atrial premature complex:** the P wave is not followed by a QRS complex (AV-His-Purkinje system in refractory period); the pause is usually noncompensatory



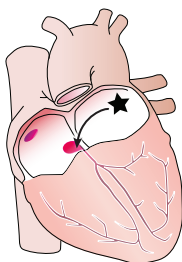
SUPRAVENTRICULAR TACHYARRHYTHMIAS



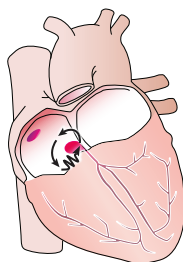
*70 msec for intracardiac VA interval (90 msec for surface ECG VA interval)



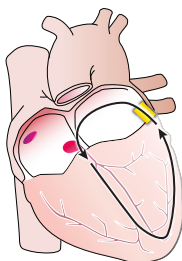
Atrial Flutter



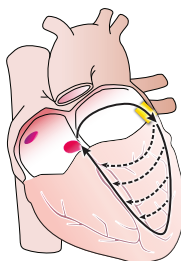
Focal atrial tachycardia



AVNRT: nodal reentry



Orthodromic AVRT



Antidromic AVRT

RESPONSE TO ADENOSINE (OR VAGAL MANEUVER)

Sudden arrest	Slowing then re-acceleration
<ul style="list-style-type: none"> • AVNRT • AVRT • SA node reentrant tachycardia • (Focal atrial tachycardia) 	<ul style="list-style-type: none"> • Sinus tachycardia • Focal atrial tachycardia • AF; Flutter • Nonparoxysmal junctional tachycardia

SINUS TACHYCARDIA

100-200 bpm (HRmax = 220 - age); nonparoxysmal (progressive onset and termination); normal P waves; secondary to sympathetic stimulation



ETIOLOGIES: fever / sepsis; hypotension; hyperthyroidism; anemia; anxiety; pain; exercise; hypovolemia; pulmonary embolism; ischemia; heart failure; shock; drugs (atropine; catecholamines; adriamycin); alcohol; cocaine; high output state; pregnancy

INAPPROPRIATE SINUS TACHYCARDIA: increased automaticity / sinus dysautonomia

- **Diagnosis:** sinus HR > 100 bpm at rest; mean 24-h HR > 90 bpm; diagnosis of exclusion (rule out physiological sinus tachycardia or focal AT from the high RA)

- > **Management:** Rule out an underlying cause (anemia; hyperT4); Ivabradine; BB; radiofrequency modification of sinoatrial node as last resort

POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS): orthostatic intolerance with significant increase of HR during the first 10 min after standing (HR > 120 bpm or HR increased by > 30 bpm)

- > **Management:** fluids; NaCl; raise the head of the bed; training; elastic stockings; BB; Fludrocortisone; Midodrine; SSRI

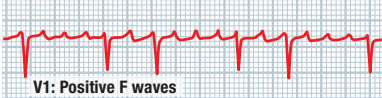
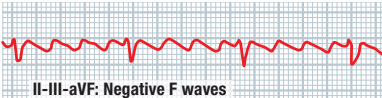
SINOATRIAL NODAL REENTRANT TACHYCARDIA (SANRT): paroxysmal tachycardia; abrupt onset; P wave identical to P wave in SR

- > **Management:** vagal maneuver; Adenosine; BB; CCB; RF ablation

ATRIAL FLUTTER

ATRIAL FREQUENCY: 300 bpm (slowed by class IC AA with risk of 1:1 conduction)

VENTRICULAR FREQUENCY: 150 or 100 or 75 bpm (2:1 or 3:1 or 4:1 conduction)

TYPICAL ATRIAL FLUTTER	ATYPICAL ATRIAL FLUTTER
<ul style="list-style-type: none"> Cavotricuspid isthmus-dependent macroreentrant flutter: atrial flutter counterclockwise around the tricuspid valve annulus (most common) versus clockwise flutter ECG: sawtooth flutter waves (regular and identical); negative waves in II-III-aVF and positive waves in V1 in counterclockwise flutter (and vice versa in clockwise flutter); 2:1 or 3:1 or 4:1 AV conduction  <p>V1: Positive F waves</p>  <p>II-III-aVF: Negative F waves</p> <p>MANAGEMENT</p> <ul style="list-style-type: none"> ECV (50 J biphasic) or atrial overdrive or CCV (IV Ibutilide) AV node blocking agents (rate control more difficult than in AF) Class IC AAD (combined with AV node blocking agent) or class III AAD Thromboembolic prevention (▶▶ AF) RF ablation of cavotricuspid isthmus: success rate: 90-95%; first-line long-term treatment; target bidirectional block; 22-50% will have AF within 30 months 	<ul style="list-style-type: none"> Cavotricuspid isthmus non-dependent macroreentrant flutter <p>1) IART (intra-atrial reentrant tachycardia): macroreentrant circuit arising around a surgical scar following cardiac surgery</p> <p>2) Left atrial flutter post-AF ablation</p> <ul style="list-style-type: none"> ECG: variable morphology of flutter waves (depending on the circuit involved) and different from that of typical flutter Management: ECV; AV node blocking agents; AAD; RF ablation

FOCAL ATRIAL TACHYCARDIA

ATRIAL FREQUENCY: 150-250 bpm

THREE MECHANISMS: **A)** Automatic (incessant); **B)** Triggered activity; **C)** Microreentrant

ORIGIN: precise focus (pulmonary vein; atrial appendage; *crista terminalis*; SVC or IVC; coronary sinus; mitral annulus; fossa ovale)

ECG: morphology of P wave different from that in SR; isoelectric segment between P waves on all leads (unlike flutter); **long RP interval**

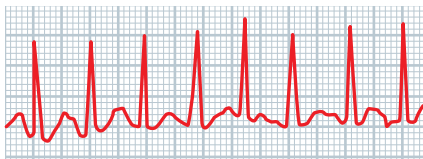
- > **V1 - Positive P wave:** = LA focus (negative P wave in aVL and I)
- > **V1 - Negative or biphasic P wave:** = RA focus (positive or biphasic P wave in aVL)

MANAGEMENT: AV node blocking agent; Class IC or III AAD; ablation of arrhythmogenic focus with 3D electroanatomic mapping (85% success)

MULTIFOCAL ATRIAL TACHYCARDIA (MAT)

ATRIAL FREQUENCY: 100-150 bpm

IRREGULARLY IRREGULAR RHYTHM: absence of dominant pacemaker; variable morphology of P waves (**≥ 3 different morphologies**); variable PR interval; abnormal automaticity



RISK FACTORS: COPD; age; Digoxin; Theophylline; hypomagnesemia

MANAGEMENT: correct underlying disease; nondihydropyridine CCB; Amiodarone; Mg^{2+}

ATRIOVENTRICULAR NODAL REENTRANT TACHYCARDIA (AVNRT)

AVNRT: 150-250 bpm; very regular rhythm (except at onset and termination)

ONSET: sudden; **APC with long PR interval (antegrade conduction via the slow pathway)**

SYMPTOMS: palpitations; anxiety; angina; syncope (↓ cardiac output; postconversion sinus pause; vasodepressive response)

TYPICAL AVNRT	ATYPICAL AVNRT
<ul style="list-style-type: none"> Antegrade conduction via the slow pathway; retrograde conduction via the fast pathway (with retrograde atrial activation) ECG: Short RP < 90 ms; retrograde P wave hidden in the QRS or just after the QRS (pseudo-r' in V1; pseudo-S in II-III-aVF; absent on baseline ECG in sinus rhythm); QRS alternans if very rapid 	<ul style="list-style-type: none"> 5-10 % Antegrade conduction via the rapid pathway; retrograde conduction via the slow pathway; long RP

MANAGEMENT: vagal maneuver (Valsalva; carotid sinus massage); Adenosine; CCB; BB; ECV (50 J biphasic); class IC AAD (combined with AV node blocking agent); RF ablation

RF ABLATION: success rate > 95%; **first-line long-term treatment** +

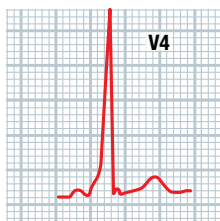
- > **Ablation of slow pathway:** inferoposterior to AV node (between the septal aspect of the tricuspid valve annulus and the ostium of the coronary sinus)
- > **Complications:** AV block (1%); recurrence (5%); tamponade

ATRIOVENTRICULAR REENTRANT TACHYCARDIA (AVRT) & ACCESSORY PATHWAY

AVRT: 150-250 bpm; very regular rhythm (except at onset)

ACCESSORY PATHWAY (BUNDLE OF KENT): connection between atrium and ventricle (at the level of the AV sulcus) short-circuiting the AV node - His-Purkinje system; **retrograde conduction only or anterograde (and retrograde) conduction** +

- 1) Accessory pathway with retrograde conduction only (30%):** hidden pathway; absence of preexcitation
 - **Associated arrhythmia:** orthodromic AVRT
- 2) Accessory pathway with anterograde conduction (70%):** ventricular pre-excitation; fusion of ventricular activations by the accessory pathway and by the AV - His-Purkinje system
 - **Short or negative HV interval** +
 - **Associated arrhythmias:** **A)** Orthodromic AVRT (retrograde conduction); **B)** Antidromic AVRT; **C)** Anterograde conduction of supraventricular arrhythmia (pre-excited AF)
 - **ECG:** PR < 120 ms; wide QRS (> 120 ms) with delta wave; ST-T abnormalities (opposite direction to the QRS); maximized pre-excitation when AV node in refractory period

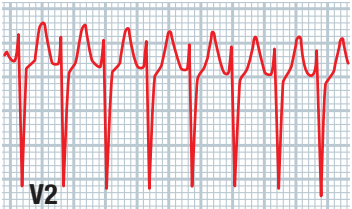
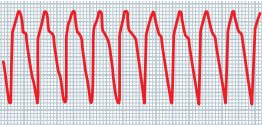


SITE OF PATHWAY	DELTA WAVE		
	V1	AVF	AVL
Left lateral	+	+	-
Left septal or posterior	+	-	+
Right septal or posterior	-	-	+
Anterior or right lateral	-	+	+

WOLFF-PARKINSON-WHITE SYNDROME: symptoms compatible with tachyarrhythmia + ventricular pre-excitation

- > **Benign pathway:** inefficient pathway with long refractory period; abrupt disappearance of pre-excitation on stress test (or intermittent loss during ECG or ambulatory monitoring)
- > **Malignant pathway:** **refractory period < 250 ms**; able to maintain effective anterograde conduction of possible AF (with risk of VF and sudden death) +

DEMONSTRATION OF AN ACCESSORY PATHWAY: **A)** Eccentric retrograde atrial activation during ventricular stimulation or during orthodromic AVRT; **B)** Ventricular stimulation during AVRT induces atrial activation even when the His bundle is refractory; **C)** Ventricular stimulation induces atrial activation before activation of the His bundle; **D)** Ventricular stimulation at various frequencies associated with a stable VA interval (non-decremental VA conduction)

ORTHODROMIC ATRIOVENTRICULAR REENTRANT TACHYCARDIA (AVRT)	ANTIDROMIC ATRIOVENTRICULAR REENTRANT TACHYCARDIA (AVRT) (5–10%)
<ul style="list-style-type: none"> • Macro-reentrant tachycardia with anterograde conduction via the AV / His–Purkinje system and retrograde conduction via the accessory pathway • ECG: Narrow QRS; retrograde P wave following QRS (short RP but > 70 ms intra-cardiac); negative retrograde P wave in lead I if left lateral bundle  <ul style="list-style-type: none"> • If functional branch block ipsilateral to the accessory pathway: ↗ VA interval and ↗ tachycardia cycle length 	<ul style="list-style-type: none"> • Macro-reentrant tachycardia with anterograde conduction via the accessory pathway and retrograde conduction via the AV / His–Purkinje system; wide QRS tachycardia 

MANAGEMENT OF AVRT: vagal maneuver; Adenosine (can precipitate AF); AV node blocking agent (can precipitate preexcited AF); ECV (50 J); AAD (IC; III); RF ablation of accessory pathway

ABLATION OF THE ACCESSORY PATHWAY: **first-line long-term treatment**; success rate: 95%

➤ **Complications:** 5% recurrence rate; vascular access; microembolism / stroke (left pathway); tamponade; AV block; coronary lesion

➤ **Asymptomatic pathway: EP study or observation is reasonable (IIa recommendation):** ablation if high risk findings during EP study (**R–R < 250 ms** during induced AF; multiple accessory pathways; AVRT precipitating pre-excited AF; pathway with refractory period < 240 ms) or in patients with specific employment (e.g. pilot)

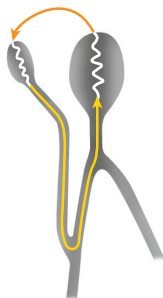
PERMANENT FORM OF JUNCTIONAL RECIPROCATING TACHYCARDIA (PJRT):

incessant supraventricular tachycardia; posteroseptal accessory pathway (R > L); pathway with **slow retrograde one-directional** conduction; **long RP**; **negative P wave in II–III–aVF**

MAHAIM PATHWAY: accessory pathway in lateral wall of RV; distal connection to RV (atrioventricular connection) or to the right branch (atriofascicular connection); **similar conduction properties to those of the AV node (decremental conduction at higher HR); anterograde conduction only**

➤ **Baseline ECG:** normal (minimal pre-excitation)

➤ **Associated arrhythmia:** antidromic AVRT (with LBBB morphology); QRS axis 0° and -75°; QRS < 150 ms; late precordial transition; HR 130–270 bpm



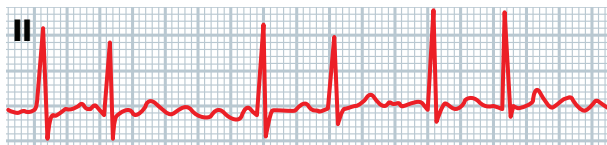
MAHAIM PATHWAY

JUNCTIONAL TACHYCARDIA

NONPAROXYSMAL JUNCTIONAL TACHYCARDIA	PAROXYSMAL JUNCTIONAL ECTOPIC TACHYCARDIA (JET)
<ul style="list-style-type: none"> 70-130 bpm; nonparoxysmal = progressive onset ("warm-up") Origin: origin of AV node or His bundle; narrow QRS; abnormal automaticity Etiologies: Digoxin poisoning; post-cardiac surgery; electrolyte disorder; ischemia; MI; COPD; hypoxia; myocarditis Management: Treatment of underlying cause; BB; CCB 	<ul style="list-style-type: none"> 110-250 bpm; paroxysmal = sudden onset; more frequent in children; triggered by exercise or stress Origin: AV node or His bundle; narrow QRS; AV dissociation versus VA association Management: BB; AAD (IC; III); RF ablation

6.4/ ATRIAL FIBRILLATION

ATRIAL FREQUENCY: 400-600 bpm; absence of organized P wave with chaotic atrial fibrillation-rhythm; irregularly irregular ventricular rhythm



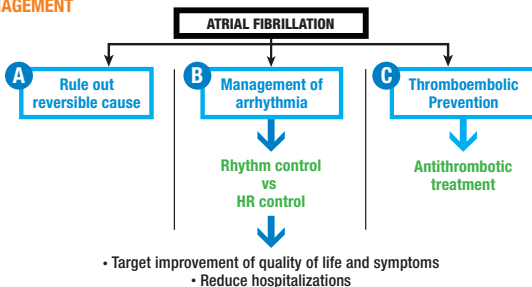
> **Lead V1:** sometimes prominent fibrillatory waves (mimicking atrial flutter), but absence of organized waves elsewhere

CLASSIFICATION

Paroxysmal AF	Terminates spontaneously or with intervention within < 7 days of onset
Persistent AF	Continuous AF, sustained > 7 days
Longstanding persistent AF	Continuous AF, sustained > 12 months
Permanent AF	No other attempt to restore and/or maintain SR
Nonvalvular AF	Absence of rheumatic MS, prosthetic heart valve or mitral valve repair

SYMPTOMS: palpitations; tiredness; dyspnea; exercise intolerance; faintness; syncope (conversion pause or rapid AF in the presence of structural heart disease); systemic embolism; heart failure (tachycardiomyopathy)

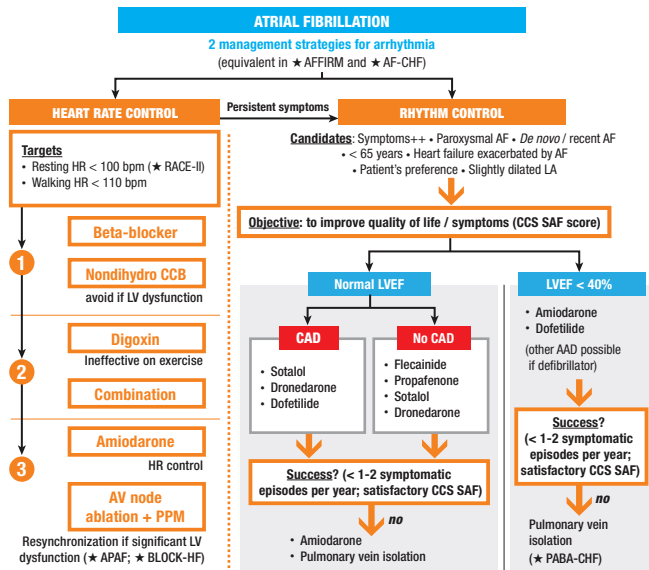
CCS SAF SCALE	
Class 0	Asymptomatic
Class I	Minimal effect on quality of life
Class II	Minor effect on quality of life
Class III	Moderate effect on quality of life
Class IV	Severe effect on quality of life



RULE OUT REVERSIBLE CAUSE AND RISK FACTORS: Alcohol ("holiday heart syndrome"); ischemia; myocarditis - pericarditis; structural heart disease / heart failure / cardiomyopathy / valvular heart disease / LVH / congenital heart disease / diastolic dysfunction; supraventricular tachycardia (tachycardia-induced AF); SSS; WPW; HTN; pulmonary embolism; hyperthyroidism; frequent V-Pace; OSAHS; vagal hypertonía (athlete; sleep); hyperadrenergism (exercise); postoperative; pneumonia; PHT

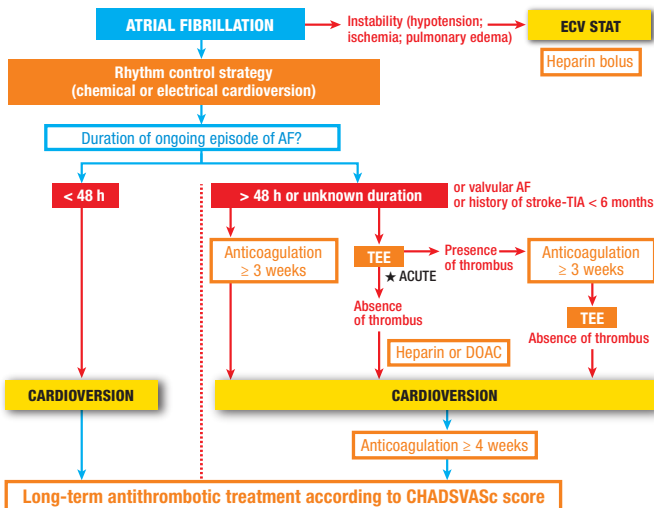
➤ **AF in young patient with structurally normal heart:** consider electrophysiological study to eliminate other supraventricular arrhythmia degenerating to AF (tachycardia-induced AF)

MANAGEMENT OF ARRHYTHMIA



HEART RATE CONTROL STRATEGY			
Diltiazem	0.25 mg/kg IV x 10 min (repeat 0.35 mg/kg PRN)	120 - 480 mg PO qd	Hypotension; bradycardia; edema; negative inotrope; avoid if ↘ LVEF or pre- excited AF
Verapamil	0.075 - 0.15 mg/kg IV x 2 min	120 - 240 mg PO bid	
Metoprolol	2.5 - 5 mg/kg IV x 2 min (3 doses every 5 min PRN)	25 - 200 mg PO bid	Hypotension; bradycardia; tiredness; depression; asthma; negative inotrope; avoid if preexcited AF
Nadolol	10 - 320 mg qd		
Esmolol	IV bolus: 500 µg/kg; Infusion: 50-300 µg/kg/min (dilution: 2500 mg / 250 mL)		
Digoxin	0.25 mg IV (or PO) every 6 h (4 doses over 24 h; adjustment according to creatinine clearance)	0.0625 to 0.25 mg qd	Digoxin toxicity; Nausea; Vomiting; Visual abnormalities; avoid in the presence of pre-excited AF
HEART RHYTHM CONTROL STRATEGY			
CLASS IC			
Flecainide	50 - 150 mg PO bid * Combine with AV node blocking agent	<ul style="list-style-type: none">• Efficacy at 1 year: 30-50 %• Adverse effects: ↗ QRS (caution if > 25%); VT; bradycardia; 1:1 flutter• Contraindications: CAD or LV dysfunction (★ CAST)• Pre-treatment stress test if > 50 years or high Framingham score	
Propafenone	50 - 300 mg PO tid * Combine with AV node blocking agent		
CLASSE III			
Amiodarone	Loading dose of 10 g over several weeks then 100 - 200 mg PO qd	<ul style="list-style-type: none">• Efficacy at 1 year: 60-70 % (★ CTAF)• Avantage: controls HR (BB effect)• Adverse effects: ➡➡➡ Amiodarone	
Dronedarone	400 mg PO bid	<ul style="list-style-type: none">• Efficacy at 1 year: 40 %• ★ ATHENA: Paroxysmal AF; ↘ cardiac mortality with Dronedarone• Contraindications: heart failure / LVEF < 40% (★ ANDROMEDA) or permanent AF (★ PALLAS) or Digoxin• Monitor LFTs at 6 months	
Sotalol	40 - 160 mg PO bid	<ul style="list-style-type: none">• Efficacy at 1 year: 30-50 % (★ CTAF)• Adverse effects: ↗ QT; torsade de pointes; bradycardia; asthma (BB effect)• Avoid: women > 65 years / CRF / LVEF < 40% / significant LVH / electrolyte disorders / ↗ QTc• Monitoring of QT for 72 h; stop if QTc > 500 ms	
Dofetilide	0.125 to 0.5 mg PO bid (according to CrCl)	<ul style="list-style-type: none">• Complication: torsade de pointes• Contraindications: CrCl < 20 mL/min; hypokalemia; baseline QTc > 440 ms	

“PILL IN THE POCKET” APPROACH: AAD as needed (Flecainide 200 to 300 mg or Propafenone 450 to 600 mg) combined with Metoprolol 50 to 100 mg; indicated in the presence of occasional episodes in subjects with a healthy heart; initiate under cardiac monitoring to demonstrate safety of the approach



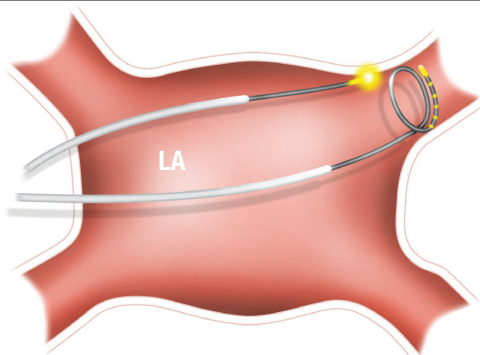
ELECTRICAL CARDIOVERSION: 200 J biphasic

- > **Failure (5 %):** Add AAD followed by another attempt of ECV (Amiodarone; Flecainide; Propafenone; Ibutilide; Sotalol)
- > **Conversion then early recurrence of AF (ERAF) post-ECV:** Add AAD followed by another attempt of ECV

CHEMICAL CARDIOVERSION: only minimally effective when AF present for > 7 days

CHEMICAL CARDIOVERSION		
Propafenone	450 to 600 mg PO	<ul style="list-style-type: none"> Hypotension; 1:1 flutter; bradycardia; complete AV block Contraindicated in the presence of CAD or systolic dysfunction; administer with AV node blocking agent
Flecainide	200 to 300 mg PO	
Procainamide	15-17 mg/kg IV x 60 min	<ul style="list-style-type: none"> Hypotension Efficacy: 60 %
Ibutilide	1 mg IV x 10 min; may repeat once if necessary	<ul style="list-style-type: none"> Torsade de pointes (2-3%) Contraindicated if LVEF < 30% or significant LVH or \nearrow QTc > 440 ms or SSS or hypokalemia Pretreat with MgSO₄
Vernakalant	3 mg/kg x 10 min then observation for 15 min then 2 nd bolus of 2 mg/kg x 10 min PRN	<ul style="list-style-type: none"> Blocks various atrial ionic channels (\nearrow refractory period) Efficacy: 50 % (★ ACT; ★ AVRO) Adverse effects: dysgeusia; Nausea; Hypotension; \nearrow QT and QRS intervals Contraindications: hypotension; ACS during previous 30 days; NYHA III or IV; Severe AS; non-corrected QT > 440 ms; LVEF ≤ 35%

PULMONARY VEIN ISOLATION



PAROXYSMAL AF	PERSISTENT AF
<ul style="list-style-type: none"> Triggered by premature complexes arising in pulmonary veins (90% of cases; ★ Haïssaguerre) Ablation: pulmonary vein isolation (electrical disconnection from the rest of the LA by radiofrequency ablation) 	<ul style="list-style-type: none"> Presence of a substrate maintaining and perpetuating the arrhythmia + Substrate: structural and electrical remodeling of the atrium; fibrosis - inflammation - ↘ refractory period Ablation: pulmonary vein isolation combined with modification of the substrate (other radiofrequency lesions in the atria) <ul style="list-style-type: none"> > Linear ablation (roof of LA and mitral annulus; ± cavotricuspid isthmus) > Ablation of complex fractionated atrial electrograms sites (CFAE) > No benefit in ★ STAR-AF

OBJECTIVE: improve symptoms and quality of life

INDICATION: **AF with persistent and harmful symptoms (negative impact on quality of life) despite trial of drug treatment (class I or III AAD)** +

SUCCESS RATE: **60-75% after 1 procedure and 75-90% after 2 procedures** (success rate 10-15% lower in the presence of persistent AF); improvement of quality of life; more effective than AAD for maintenance of SR

MAJOR COMPLICATIONS: **5 %**; vascular complication (1-2%); cardiac perforation / tamponade (1%); thromboembolism (1%); PV stenosis (0.5%); atrio-esophageal fistula; phrenic nerve palsy (diaphragmatic paralysis); atypical flutter; death (1/1,000)

CONTRAINDICATIONS: LA > 55 mm; significant structural heart disease; LA thrombus; long-term AF; mechanical MVR

PERIPROCEDURAL CONSIDERATIONS: TEE before the procedure; procedure performed under anticoagulation (continue warfarin; stop DOAC 12-24 h before the procedure); continue anticoagulation for 2 months post-op (then according to CHADS₂VASc score)

> **Early recurrence of AF post-PVI (< 3 months):** secondary to acute inflammation; management by rhythm control then re-evaluate at 3 months

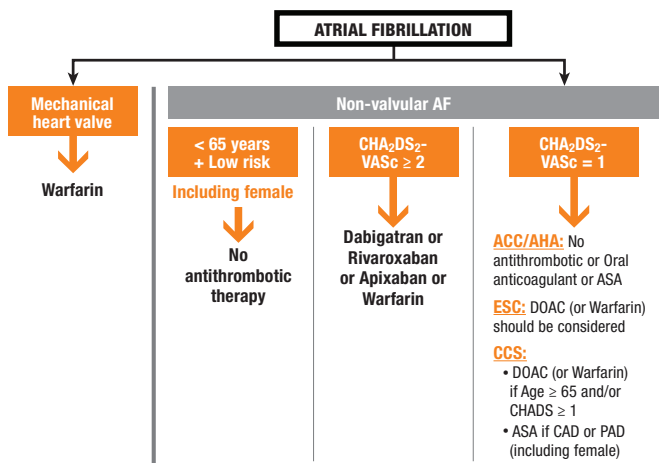
PVI FOR PERSISTENT AF AND HEART FAILURE: more effective than AV node ablation

+ resynchronization (★ PABA-CHF)

- ★ **AATAC-AF:** PVI superior to Amiodarone in relieving persistent AF in patients with congestive heart failure; PVI associated with ↓ all-cause mortality and ↓ hospitalization

SURGICAL ABLATION OF AF: indicated for symptomatic AF when concomitant cardiac surgery is planned

- ▶ **Paroxysmal AF: pulmonary vein isolation** (endocardial or epicardial) ± ablation line to mitral annulus
- ▶ **Persistent AF: modified Cox-Maze procedure;** requires bilateral atriotomy; ablation lines in LA to isolate pulmonary veins / isolate the posterior LA / create an ablation line between the pulmonary veins and mitral annulus; ablation lines at the cavotricuspid isthmus and between inferior and superior venae cavae; left atrial appendectomy; one-year success rate: 85% (63% in ★ CTSN AF)

THROMBOEMBOLIC PREVENTION

CHADS ₂ SCORE		
Congestive heart failure and/or LVEF ≤ 40%	1 point	Stroke / year 0 → 1.9 %
HTN	1 point	1 → 2.8 %
≥ 75 years	1 point	2 → 4.0 %
DM	1 point	3 → 5.9 %
Stroke – TIA – Thromboembolism	2 points	4 → 8.5 %
		5 → 12.5 %
		6 → 18.2 %

Gage BF, Waterman AD, Shannon W, et al. JAMA 2001;285:2864-70.

CHA ₂ DS ₂ -VASC SCORE		
Recent decompensated HF and/or LVEF ≤ 40%	1 point	Stroke / year 0 → 0 % 1 → 1.3 % 2 → 2.2 % 3 → 3.2 % 4 → 4.0 % 5 → 6.7 % 6 → 9.8 % 7 → 9.6 % 8 → 6.7 % 9 → 15.2 %
HTN	1 point	
≥ 75 years	2 points	
DM	1 point	
Stroke - TIA - Thromboembolism	2 points	
Vascular disease (history of MI; PAD; Aortic plaque)	1 point	
65-74 years	1 point	
Female	1 point	

Lip GY, Nieuwlaar R, Pisters R, et al. Chest 2010;137:263-272.

BENEFIT OF WARFARIN IN PRIMARY PREVENTION: ★ AFASAK-1 AND 2; ★ SPAF-1 and 2 and 3; ★ BAATAF; ★ CAFA; ★ SPINAF

➤ **Benefit of Warfarin:** relative risk of stroke ↘ by 64%

+

➤ **Benefit of ASA:** relative risk of stroke ↘ by 19%

WARFARIN ANTIDOTE: vitamin K; prothrombin complex concentrate (Octaplex; Beriplex; Cofact; Proplex; factors II - VII - IX - X); FFP (8 units)

★ **ACTIVE-A:** Warfarin impossible; ASA + Plavix vs ASA; ↘ stroke but ↗ major bleeding

➤ **Indication for ASA-Clopidogrel:** when any form of oral anticoagulation is impossible but acceptable bleeding risk

BLEEDING RISK ASSOCIATED WITH ANTICOAGULATION

WARFARIN: annual risk of major bleeding ≈ 3%

+

HAS-BLED SCORE		
HTN (SBP > 160 mmHg)	1 point	Major bleeding/year 0 → 1.1 % 1 → 1.02 % 2 → 1.88 % 3 → 3.74 % 4 → 8.7 % 5 → 12.5 %
Abnormal (liver or renal function) • Creatinine ≥ 200 μmol/L or Dialysis • AST - ALT > 3 x ULN or Bilirubin 2 x ULN or Cirrhosis	1 point each	
Stroke	1 point	
Bleeding (history; Anemia; Bleeding diathesis)	1 point	
Labile INR	1 point	
Elderly (> 65 years)	1 point	
Drugs (associated with a risk of bleeding) or Alcohol	1 point each	

Pisters R, Lane DA, Nieuwlaar R, et al. Chest 2010;138:1093-100.

HAS-BLED ≥ 3: high bleeding risk; try to correct reversible risk factors

OTHER SCORES: HEMORR₂HAGES; ATRIA

DIRECT ORAL ANTICOAGULANTS (DOAC)

CONTRAINDICATED: **A)** Mechanical prosthetic valve; **B)** Moderate to severe mitral stenosis (usually of rheumatic origin)

DABIGATRAN (PRADAXA)	RIVAROXABAN (XARELTO)	APIXABAN (ELIQUIS)	EDOXABAN (SAVAYSA; LIXIANA)
Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Dose: 150 mg bid • 110 mg bid: ≥ 75 years; CrCl 30-49 mL/min with additional bleeding risk factor Not studied in patients with CrCl < 30 mL/min	Dose: 20 mg qd • 15 mg qd: CrCl 30-49 mL/min Not studied in patients with CrCl < 30 mL/min	Dose: 5 mg bid • 2.5 mg bid: ≥ 2 factors (≥ 80 years or ≤ 60 kg or creatinine ≥ 133 µmol/L) Not studied in patients with CrCl < 25 mL/min	Dose: 60 mg qd • 30 mg qd: CrCl 30-49 mL/min Not studied in patients with CrCl < 30 mL/min
★ RELY • 150 mg bid: ↘ stroke (superior to warfarin); comparable bleeding • 110 mg bid: non-inferior for stroke; ↘ bleeding	★ ROCKET-AF • 20 mg (15 mg if CrCl 30-49 mL/min): non-inferior to warfarin for stroke; comparable bleeding	★ ARISTOTLE • Apixaban 5 mg bid (2.5 mg bid not extensively studied): ↘ stroke (superior to warfarin); ↘ bleeding; ↘ all-cause mortality	★ ENGAGE-AF • 60 mg qd: non-inferior for stroke (trend for superiority); ↘ bleeding • 30 mg qd: non-inferior for stroke (trend for inferiority); ↘ bleeding; ↘ all-cause mortality
Renal excretion: 80%	Renal excretion: 33%	Renal excretion: 25%	Renal excretion: 50%

FOLLOW-UP: CrCl (Cockcroft-Gault) prior to initiation / when clinically indicated / ≥ 1 x / year

CONSIDER REDUCED DOSE: high bleeding risk (HAS-BLED ≥ 3); impaired renal function; drug interactions (P-gp and/or CYP3A4)

★ AVERROES: AF with mean CHADS = 2; Warfarin impossible; Apixaban 5 mg bid versus ASA; early discontinuation (↘ stroke with Apixaban; similar bleeding)

BLEEDING WITH DOAC: Idarucizumab (Dabigatran; ★ RE-VERSE); Andexanet alpha (Rivaroxaban; Apixaban; Edoxaban); discontinue the anticoagulant; local compression; plasma expansion / transfusion; maintain diuresis to promote elimination; seek an opinion from a hematologist / pharmacist; consider prothrombin complex concentrates or activated factor VII or hemodialysis (Dabigatran)

DOAC AND OTHER ANTICOAGULANTS	
Switch from Warfarin → DOAC	• INR < 2.0 → Start DOAC immediately • INR 2.0 - 2.5 → Start DOAC on the following day
Switch from IV Heparin → DOAC	After stopping heparin
Switch from LMWH → DOAC	At the next scheduled dose of LMWH
Switch from DOAC → LMWH or IV Heparin	At the next scheduled dose of DOAC
Switch from DOAC → Warfarin	Stop DOAC when INR > 2.0

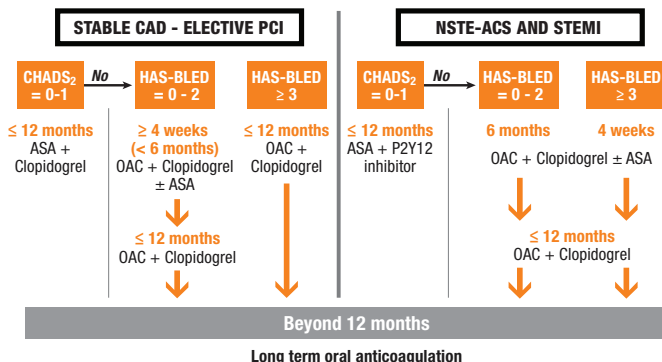
PERIOPERATIVE USE OF DOAC	
Surgery with low bleeding risk (Dental extraction; cataract; endoscopy without biopsy; superficial skin surgery)	Continue DOAC (operate under DOAC) or skip the dose in the morning of the operation
Surgery with intermediate bleeding risk (Endoscopy with biopsy; prostate or bladder biopsy; angiography; electrophysiological intervention; pacemaker)	<ul style="list-style-type: none"> • Apixaban – Rivaroxaban: stop DOAC ≥ 24 h before the operation • Dabigatran: stop DOAC ≥ 24 h (CrCl ≥ 80 mL/min) or ≥ 36 h (CrCl 50-80 mL/min) or ≥ 48 h (CrCl 30-50 mL/min)
Surgery with high bleeding risk (Lumbar puncture; spinal / epidural surgery; thoracic / abdominal / neurological / orthopedic surgery; liver or kidney biopsy; TURP)	<ul style="list-style-type: none"> • Apixaban – Rivaroxaban: stop DOAC ≥ 48 h before the operation • Dabigatran: stop DOAC ≥ 48 h (CrCl ≥ 80 mL/min) or ≥ 72 h (CrCl 50-80 mL/min) or ≥ 96 h (CrCl 30-50 mL/min)

PERCUTANEOUS OCCLUSION OF LEFT ATRIAL APPENDAGE

★ **PROTECT AF:** Watchman system non-inferior to warfarin for thromboembolic prevention; associated procedural complications; requires long-term antiplatelet therapy

INDICATION: high risk of stroke (CHADS₂ ≥ 2) for whom anticoagulation is precluded

ATRIAL FIBRILLATION AND CORONARY ARTERY DISEASE

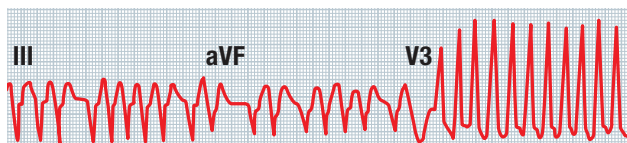


OAC (Oral anticoagulation):
Either Warfarin (INR 2.0 - 2.5) or DOAC (Dabigatran 110 mg bid;
Rivaroxaban 15 mg qd; Apixaban 2.5 mg bid)

Proton pump inhibitor if risk of GI bleeding

★ **WOEST:** 573 patients with an indication for anticoagulant therapy undergoing PCI (25-30% with ACS); Warfarin + Clopidogrel (versus Warfarin + Clopidogrel + ASA) associated with ↓ bleeding and ↓ mortality

PRE-EXCITED ATRIAL FIBRILLATION



Irregularly irregular tachycardia with wide QRS

COMPLICATIONS: rapid AV conduction via an efficient accessory pathway (refractory period < 250 ms) → transformation to VF

MANAGEMENT: ECV stat; Procainamide or Ibutilide if hemodynamically stable; ablation of accessory pathway

➤ **Agents contraindicated:** AV node blocking agents predisposing to conduction via the accessory pathway (Digoxin; nondihydropyridine CCB; BB; Adenosine; IV Amiodarone)

AF DETECTED BY PACEMAKER (SUBCLINICAL AF)

★ **ASSERT:** detection of subclinical atrial tachycardia (defined by HR > 190 bpm and duration > 6 min) associated with increased thromboembolic risk

➤ **Episode > 17.7 h (upper quartile of duration):** significantly ↑ risk of stroke (fivefold)

★ **TRENDS:** atrial tachycardia (probable AF) ≥ 5.5 h associated with increased thromboembolic risk

CONSIDER ANTICOAGULATION: **A)** Episode lasting ≥ 24 h; **B)** Shorter episode in high-risk patient (cryptogenic stroke; TIA)

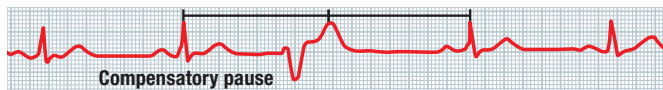
6.5/ VENTRICULAR TACHYARRHYTHMIAS

PREMATURE VENTRICULAR COMPLEXES

Premature ventricular depolarization during the cardiac cycle; wide QRS; T wave in opposite direction to the QRS

MODIFIERS: couplet; bigeminy; trigeminy; monomorphic; polymorphic; associated with compensatory or noncompensatory pause; associated with retrograde atrial activation; interpolated complex; fusion complex; associated with echo (PVC → retrograde atrial activation → anterograde ventricular activation)

➤ **Compensatory pause:** interval between QRS before and after PVC = 2 x RR interval (failure of PVC to reset the sinoatrial node)



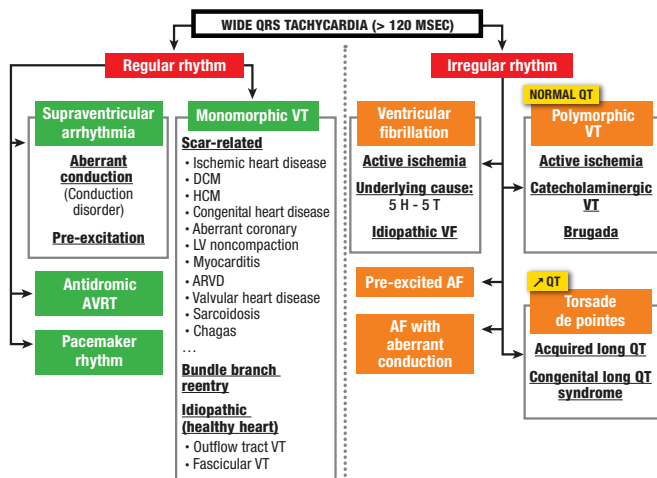
➤ **Interpolated PVC:** PVC between two beats of baseline rhythm with no modification of rhythm

PVC / MONOMORPHIC NSVT IN STRUCTURALLY NORMAL HEART: benign; risk of tachycardiomyopathy if frequent (> 10,000 / 24 h) and with a short coupling interval (< 300 ms)

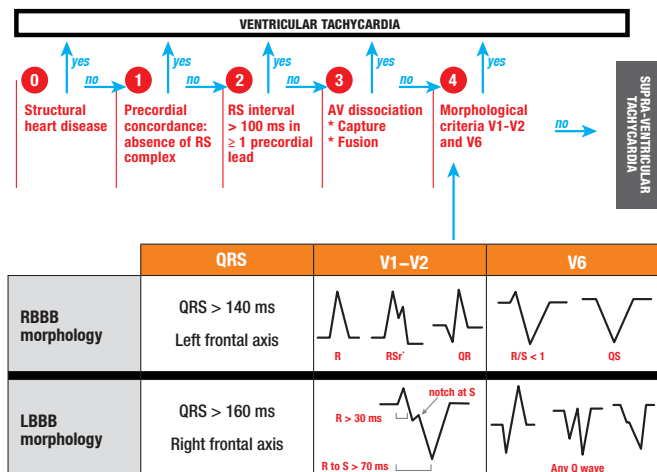
MANAGEMENT: Observation; intervention if symptoms or complications (tachycardiomyopathy); BB; AAD (IC; III); radiofrequency ablation

PVC ASSOCIATED WITH AF: elements in favor of PVCs rather than aberrant conduction → fixed coupling interval / pause after wide QRS / bigeminy

WIDE QRS TACHYCARDIA: DIFFERENTIAL DIAGNOSIS



WIDE QRS TACHYCARDIA: VT VERSUS ABERRANT CONDUCTION



OTHER CRITERIA

- **Supraventricular tachycardia with aberrant conduction:** **A)** Onset: Early P wave (APC); **B)** Change of PP interval precedes change of RR interval; **C)** QRS: identical to baseline rhythm; **D)** Stopped by vagal maneuver
- **Ventricular tachycardia:** **A)** Onset: Early QRS (PVC); **B)** Change of RR interval precedes change of PP interval; **C)** QRS: identical to PVC on baseline rhythm; **D)** Canon A wave; variable intensity of S₁; variable SBP; **E)** -90° to 180° axis deviation

LOCALIZATION OF VT ON ECG

- 1) **V1 morphology:** LBBB (VT arises in RV and sometimes in LV septum); RBBB (VT arises in LV)
- 2) **Frontal axis:** Superior (VT arises in inferior wall); Inferior (VT arises in anterior wall)
- 3) **QRS V1 to V6:** **A)** Positive concordance → basal focus; **B)** Early QRS transition (V1-V2) → apical focus; **C)** Late QRS transition → midventricular focus
- 4) **QS complexes:** indicate the territory in which the arrhythmia arises (II-III-aVF = inferior; V4-V5-V6 = apical)
- 5) **Epicardial VT:** pseudo-Delta wave (initial portion of wide QRS)

VENTRICULAR TACHYCARDIA (VT)

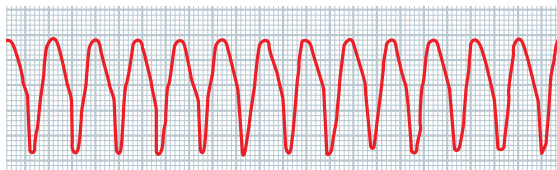
≥ 3 consecutive ventricular complexes; HR 110-250 bpm

- **Sustained:** > 30 s (or ECV necessary)
- AV dissociation or VA association (retrograde conduction)

+

MONOMORPHIC VENTRICULAR TACHYCARDIA: scar-related in the majority of cases; look for structural heart disease

+



- **Acute management:** cardioversion (100 J biphasic) / defibrillation if absent pulse (200 J biphasic); Procainamide or Amiodarone (150 mg IV x 10 min then 1 mg/min x 6 h then 0.5 mg/min x 18 h) or Sotalol; ventricular overdrive; look for underlying cause
- **Secondary prevention:** First-line ICD; BB; Amiodarone (★ OPTIC); Sotalol; Mexiletine; RF ablation if repeated ICD shocks

VENTRICULAR TACHYCARDIA IN STRUCTURALLY NORMAL HEART

►► Idiopathic ventricular tachycardia

BUNDLE BRANCH REENTRY TACHYCARDIA: in DCM; macro-reentry with anterograde conduction via the right bundle branch and retrograde conduction via the left bundle branch; Monomorphic VT with LBBB morphology

- **Management:** right bundle branch ablation

ACCELERATED IDIOVENTRICULAR RHYTHM (AIVR): 50-110 bpm; competition between sinoatrial node and a ventricular ectopic focus; increased automaticity; progressive onset and termination; associated with MI / reperfusion or Digoxin toxicity

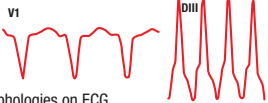

- **Management:** observer; atropine PRN; « overdrive » auriculaire

POLYMORPHIC VENTRICULAR TACHYCARDIA WITH NORMAL QT: occurs during active myocardial ischemia or in genetic arrhythmia syndrome (►► Channelopathies)

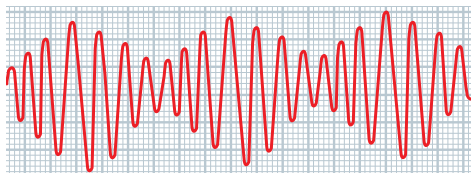
- **Acute management:** defibrillation; Rule out active ischemia; BB; Amiodarone; Lidocaine; correct electrolyte disorders

IDIOPATHIC MONOMORPHIC VENTRICULAR TACHYCARDIA

Absence of structural heart disease; favorable prognosis

<p>Outflow tract VT</p>	<p>MECHANISM: myocyte calcium overload inducing triggered activity (delayed afterdepolarization); NSVT > sustained VT; 140-180 bpm; induced by exercise / stress / Isoproterenol</p> <p>RVOT VT: LBBB morphology; inferior frontal axis; V3-V4 precordial transition</p> <p>> DDx: ARVD (abnormal SAEKG / TTE / EPS)</p> <p>> Management: Adenosine; BB; Verapamil; class IC AAD; RF ablation (90% success rate)</p>  <p>LVOT VT: 2 morphologies on ECG</p> <ol style="list-style-type: none"> 1) RBBB - Inferior axis - S in V6 2) LBBB - Inferior axis - early precordial R wave transition (V2 LVOT versus ≥ V3 RVOT) <p>VT ARISING IN SINUS OF VALSALVA: LBBB; inferior axis</p> <p>> Left sinus of Valsalva: rS in I; V1 with "w" pattern or notch; early precordial transition</p> <p>> Right sinus of Valsalva: large R wave in V1; early precordial transition</p>
<p>Fascicular VT</p>	<p>MECHANISM: reentry in Purkinje system</p> <p>3 TYPES:</p> <p>> Left posterior hemibranche: RBBB; Left superior frontal axis</p>  <p>> Left anterior hemibranche: RBBB; Right inferior frontal axis</p> <p>> High septum: Narrow QRS; normal axis</p> <p>MANAGEMENT: Verapamil / Diltiazem; class III AAD; RF ablation</p>
<p>Mitral annulus</p>	<p>ECG: RBBB morphology; Dominant R in precordial leads</p>

TORSADE DE POINTES



Polymorphic ventricular tachycardia; HR 200-250 bpm; twisting of QRS around the isoelectric line (axis changes by 180° every 5-20 beats)

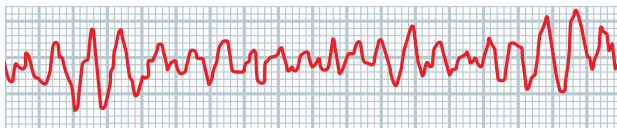
- > **Associated with** \nearrow **QT interval:** prolonged ventricular repolarization; QT > 500 ms; \pm prominent U wave
- > **Mechanism:** triggered activity (early afterdepolarization)
- > **Long RR - short RR sequence**

ETIOLOGIES - ACQUIRED LONG QT: Drugs (www.qtdrugs.org); AAD (IA; III); severe bradycardia; electrolyte disorders (hypokalemia; hypomagnesemia); CNS lesion; ischemia; hypothermia; anorexia; hypothyroidism; heart failure

- > **Congenital long QT syndrome:** \gg Channelopathies

MANAGEMENT: Mg^{2+} (1-2 g IV); ventricular overdrive; Isoproterenol (pause-dependent TdP); Lidocaine; BB with temporary pacemaker in place; correct underlying cause / correct electrolyte disorders; PPM (in the case of pause-dependent TdP)

VENTRICULAR FIBRILLATION (VF)



Chaotic ventricular rhythm; HR 400-600 bpm; absence of organized QRS - ST - T; fatal within 3-5 min

ACUTE MANAGEMENT: immediate defibrillation (200 J biphasic) \pm CPR (\gg Chapter 9); rule out ischemia; look for underlying cause ("5 H and 5 T"); AAD to prevent recurrence (Amiodarone; Lidocaine; Procainamide)

- > **5 H - 5 T:** Hypovolemia; Hypoxia; Hydrogen (acidosis); Hypokalemia / Hyperkalemia; Hypothermia; Tension pneumothorax; Tamponade; Toxin; coronary Thrombosis; pulmonary Thrombosis

ELECTRICAL STORM: \geq 3 episodes of VT/VF in 24 hours

- > **Management:** first-line BB; intubation / sedation; rule out ischemia or underlying cause; magnet over the ICD if inappropriate shocks; Amiodarone or Procainamide or Lidocaine (in the presence of ischemia); ventricular overdrive; reprogramming of ICD therapies; RF ablation; ventricular mechanical support

IDIOPATHIC VENTRICULAR FIBRILLATION

DIAGNOSIS OF EXCLUSION: absence of structural heart disease and absence of an identifiable channelopathy

EARLY REPOLARIZATION (HAÏSSAGUERRE PATTERN): association between VF and early repolarization (J point elevation \geq 1 mm on 2 contiguous inferior and/or lateral leads)

POSSIBLE MECHANISM: triggered by PVC with short coupling interval (arising in Purkinje system)

MANAGEMENT: ICD; Isoproterenol for electrical storm; Quinidine; catheter ablation of PVCs triggering VF; assessment of first-degree relatives

6.6/ CHANNELOPATHIES

CONGENITAL LONG QT SYNDROME (LQTS)

ABNORMAL QT: QTc \geq 450 ms (male) or \geq 460 ms (female)


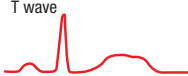
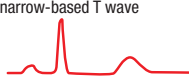
> 50th percentile of LQTS cohorts: QTc > 480 ms

+

TRANSMISSION: autosomal dominant form (Romano-Ward syndrome) or recessive form (deafness; Jervell & Lange-Nielsen syndrome)

SCHWARTZ SCORE		
ECG	Clinical features	Family history
<ul style="list-style-type: none"> • QTc \geq 480 ms: 3 points • QTc 460-479 ms: 2 points • QTc > 450-459 ms (male): 1 point • QTc after 4 min of recovery on stress test \geq 480 ms: 1 point • TdP: 2 points • Alternating T wave: 1 point • Notched T wave on 3 leads: 1 point 	<ul style="list-style-type: none"> • Syncope on exercise / stress: 2 points • Syncope without stress: 1 point 	<ul style="list-style-type: none"> • Family member with LQTS: 1 point • Sudden death in first degree relative before the age of 30 years: 0.5 point
<p>\leq 1 point: low probability 1.5 to 3 points: intermediate probability \geq 3.5 points: high probability</p>		

Schwartz PJ, Moss AM, Vincent GM, et al.
Circulation 1993; 88: 782-784.

LQT1	LQT2	LQT3
KCNQ1 mutation	KCNH2 mutation	SCN5A mutation
Trigger: exercise; swimming; stress	Trigger: noise / alarms; postpartum	Trigger: rest / sleep
Wide-based T wave 	Notched or biphasic T wave 	Long isoelectric segment then narrow-based T wave 
Management: first-line BB (significant protection); \pm ICD	Management: BB (moderate protection); \pm ICD	Management: Mexiletine; Flecainide; Ranolazine; Low protection by BB; \pm ICD

COMPLICATIONS: syncope; TdP; sudden death

MANAGEMENT: avoid trigger; avoid drugs that \nearrow QT; correct electrolyte; avoid strenuous exercise; BB (first-line); DDD or AAI pacemaker for pause-dependent TdP (especially associated with LQT3); sympathectomy

> **Risk factors for sudden death:** syncope; QTc > 500 ms; complex ventricular arrhythmia; Jervell and Lange-Nielsen

> **ICD:** **A)** Secondary prevention of sudden death; **B)** Syncope on BB therapy

SHORT QT SYNDROME (SQTS)

ECG: QTc interval \leq 340 ms with HR < 100 bpm; high amplitude T wave; short or absent ST segment

+

COMPLICATIONS: AF; syncope; VF; sudden death

DIFFERENTIAL DIAGNOSIS: hyperkalemia; hypercalcemia; hyperthermia; acidosis; Digoxin

MANAGEMENT: Quinidine; Sotalol; ICD for secondary prevention

BRUGADA SYNDROME

TRANSMISSION: autosomal dominant; sodium channel gene mutation (SCN5A; 20% of patients) or unidentified mutation

DIAGNOSTIC CRITERIA

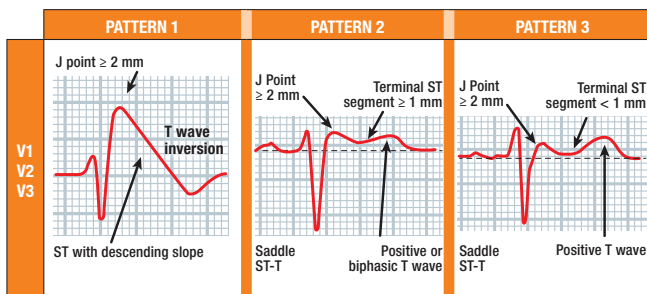
- Pattern 1 on ECG (≥ 2 leads: V1-V2-V3); spontaneous or with drug challenge (sodium channel blocking agent) or
- Pattern 2 or 3 (≥ 2 leads: V1-V2-V3) with conversion to Pattern 1 with drug challenge



≥ 1 CLINICAL CRITERIA

- Polymorphic VF or VT
- Family history of sudden death < 45 years
- Pattern 1 in the family
- VT during programmed stimulation
- Unexplained syncope
- Nocturnal agonal respiration

Wilde AA, Antzelevitch C, Borggreffe M et al. *Circulation* 2002; 106: 2514-2519.



UNMASKED BRUGADA SYNDROME: sodium channel blocking agent (challenge with Procainamide 10 mg/kg IV x 10 min or Flecainide 400 mg PO); Drugs (www.brugadadrugs.org); fever; hypokalemia or hyperkalemia; leads V1-V2-V3 in 2nd or 3rd intercostal space; Cocaine; alcohol

COMPLICATIONS: Polymorphic VT (triggered by rest / sleep) / VF; sudden death (particularly in men in their forties); AF; SSS; conduction disorder

MANAGEMENT: Quinidine and/or Isoproterenol for electrical storm

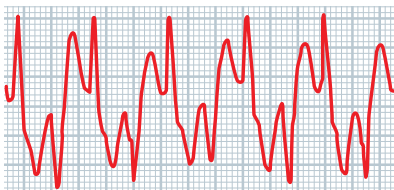
> **ICD: A)** Secondary prevention of sudden death; **B)** Spontaneous pattern 1 with syncope

CATECHOLAMINERGIC POLYMORPHIC VT

TRANSMISSION: autosomal dominant (ryanodine receptor gene mutation - RyR2) or autosomal recessive (calsequestrin gene mutation - CASQ2)

MYOCYTE CALCIUM OVERLOAD: triggered activity with delayed afterdepolarization

PRESENTATION: Polymorphic VT induced by exercise / stress; bidirectional VT



DIAGNOSIS: structurally normal heart; normal ECG

➤ **Exercise** → bidirectional VT and/or polymorphic PVCs and/or polymorphic VT

MANAGEMENT: BB (first-line treatment; Nadolol 1-2 mg/kg); CCB (Verapamil); Flecainide; Sympathectomy; avoid vigorous exercise

➤ **Titration of drug treatment:** guided by stress test and Holter

➤ **ICD: A)** Secondary prevention of sudden death; **B)** Syncope on BB therapy

GENETIC TESTING FOR FAMILIAL ARRHYTHMIAS

OBJECTIVE: A) Family screening; **B)** Establish / confirm a diagnosis

DISEASE	GENE	INDICATIONS FOR GENETIC TESTING
Long QT syndrome	Identification of a causal mutation: 75% (KCNQ1; KCNH2; SCN5A; KCNE1; KCNE2)	a) Cardiac arrest + long QT (family screening) b) Syncope + long QT (family screening / diagnosis / treatment) c) Asymptomatic long QT (family screening / diagnosis / treatment)
Brugada syndrome	Identification of a causal mutation: 20% (SCN5A)	a) Cardiac arrest + Brugada syndrome (family screening) b) Syncope + Brugada syndrome (family screening) c) Asymptomatic + Pattern 1 (family screening)
ARVD – Arrhythmogenic RV dysplasia	Identification of a causal mutation: 50% (PKP2; DSP; ± DSG2 - DSC2)	a) ARVD satisfying diagnostic criteria (family screening) b) Suspected ARVD (diagnostic criterion)
Catecholaminergic polymorphic VT	Identification of a causal mutation: 50% (RYR2; ± CASQ2)	Suspected catecholaminergic polymorphic VT (family screening)
Hypertrophic cardiomyopathy	Identification of a causal mutation: 50% (MYH7; MYBPC3; ± TNNT2 - TNNI3 - TMP1)	a) HCM with clinical diagnosis (family screening) b) HCM with pre-excitation (PRKAG2; LAMP2; GLA)
Familial dilated cardiomyopathy	Identification of a causal mutation: 20 % (MYBPC3; MYH7; TNNT2; LMNA; SCN5A)	a) Probable familial DCM (family screening) b) Familial DCM + high-grade conduction disorder / atrial arrhythmia: LMNA and SCN5A
Sudden death	Indication for targeted genetic testing: negative autopsy in the presence of familial clinical signs of a particular phenotype (for family screening)	

6.7/ SYNCOPE

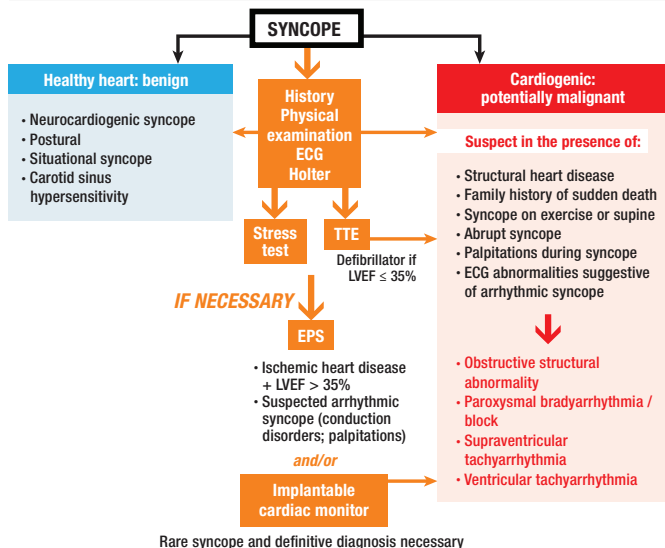
Brief loss of consciousness secondary to transient global cerebral hypoperfusion; resolves spontaneously; rapid recovery

DDX OF LOSS OF CONSCIOUSNESS: Syncope; Aborted cardiac arrest; Epilepsy; Conversion / Psychogenic; Ischemic (vertebrobasilar TIA); Migraine; Metabolic disorder (Hypoglycemia; Poisoning; Hypoxemia; Hyperventilation); Traumatic (cerebral commotion)

DDX OF SYNCOPE: **A)** Neurocardiogenic (vasovagal); **B)** OH (dysautonomia; drugs; dehydration; alcohol); **C)** Cardiogenic syncope; **D)** Carotid sinus hypersensitivity; **E)** Situational syncope (cough; defecation; laughing; micturition; postprandial; deglutition); **F)** Subclavian steal syndrome

DDX OF CARDIOGENIC SYNCOPE: Bradyarrhythmia / Block (AV block; SSS; pause following conversion of supraventricular tachyarrhythmia); Tachyarrhythmia (supraventricular; AF; WPW syndrome; VT; channelopathy; arrhythmogenic drugs; idiopathic VF); Obstructive valvular heart disease; Aortic dissection; Myxoma; Tamponade; HCM; Infarction / Ischemia; Congenital coronary artery anomalies; Massive pulmonary embolism; PHT; Pacemaker dysfunction

ASSESSMENT



ASSESSMENT: History of the present illness; Physical examination; BP supine - standing; carotid sinus massage; ECG; Holter (weekly syncope) or Loop recorder (monthly syncope); TTE

ECG ABNORMALITIES SUGGESTIVE OF ARRHYTHMIC SYNCOPE: diurnal sinus bradycardia < 40 bpm or diurnal sinus pauses ≥ 3 s; bifascicular block; QRS > 120 ms; Mobitz II or 3rd degree AV block; pre-excitation; NSVT; long QT; short QT; Brugada pattern; epsilon wave / T wave inversion in V1-V2-V3; early repolarization; LVH (dilated cardiomyopathy or HCM); Q waves

ELECTROPHYSIOLOGICAL STUDY: placement of intracardiac catheters to evaluate: **A)** sinoatrial node function (rule out SSS); **B)** AV node and His-Purkinje system function (rule out AV block); **C)** susceptibility to supraventricular and ventricular tachyarrhythmias

- > **Indications (syncope):** **A)** Ischemic heart disease not meeting the criteria for ICD; **B)** Conduction disorder with suspected arrhythmic syncope (not meeting the criteria for permanent pacemaker); **C)** Abrupt syncope or preceded by palpitations with suspicion of an arrhythmic cause
- > **Look for:** **A)** CSNRT > 525 ms; **B)** HV interval > 100 ms; **C)** Infra-His block during RA stimulation; **D)** Induced supraventricular tachycardia with hypotension; **E)** Monomorphic VT induced during programmed ventricular stimulation in the presence of ischemic heart disease
- > **Programmed ventricular stimulation:** runs of 8 successive impulses (CL between 600 and 400 ms) then 1 or 2 or 3 premature complexes (minimal coupling interval of 200 ms)

ORTHOSTATIC HYPOTENSION (OH)

DEFINITION: reduction of SBP > 20 mmHg or DBP > 10 mmHg on standing up (< 3 min) +

ETIOLOGIES: Drugs; Dehydration / Hemorrhage; Postprandial; Dysautonomia

- > **Primary dysautonomia:** **A)** Pure dysautonomia (Bradbury-Eggleston syndrome); **B)** Multi-system atrophy (Shy-Drager syndrome); **C)** Parkinson's disease
- > **Secondary dysautonomia:** DM; amyloidosis; alcohol; CRF; age; Guillain-Barré; mixed connective tissue disease; RA; Eaton-Lambert syndrome; SLE; carcinomatous autonomic neuropathy; multiple sclerosis; Wernicke's encephalopathy; hypothalamic or mesencephalic neoplastic or vascular disease; hereditary neuropathy; HIV; Chagas; Syphilis; botulism; Fabry; Tangier; vitamin B12 deficiency; porphyria; spinal cord lesion

MANAGEMENT: education; stand up slowly; lie down in the case of symptoms; sodium supplement (NaCl 1-2 g tid) and adequate hydration (2-3 L per day); avoid hypotensive drugs / alcohol; elastic compression stockings; Midodrine (alpha-agonist; 2.5-10 mg tid); Fludrocortisone (mineralocorticoid; 0.1-0.3 mg qd); raise the head of the bed by 10° to decrease nocturnal diuresis

NEUROCARDIOGENIC SYNCOPE (VASOVAGAL)

PRESENTATION: Trigger factor (prolonged standing or emotional stress) → prodromal symptoms preceding syncope (nausea; diaphoresis; blurred vision; palpitations; faintness) → brief syncope

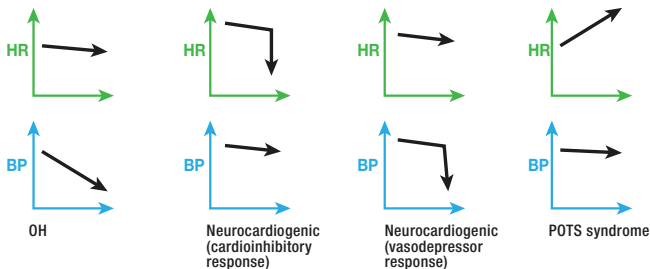
MECHANISM: vigorous ventricular contraction in the presence of low preload (secondary to venous pooling) → activation of cardiac mechanoreceptors → vagal hypertonia

- > **Three responses to vagal hypertonia:** **A)** Cardioinhibitory (sinus pause and/or AV block); **B)** Vasodepressor; **C)** Mixed

TILT TABLE TEST: indication → to confirm the diagnosis of neurocardiogenic syncope when in doubt

- > **Procedure:** 20 min in horizontal supine position → 30 to 45 min at 70° (± Isoproterenol or TNT)
- > **Look for:** syncope + type of response following vagal hypertonia

MANAGEMENT: education; avoid trigger factors; sodium supplement (1-2 g NaCl tid) and adequate hydration; elastic compression stockings (30 mmHg); avoid hypotensive drugs / alcohol; isometric counterpressure maneuvers (handgrip for 2 min; leg crossing) or supine position in the case of prodromal symptoms; orthostatic training; raise the head of the bed by 10°; Midodrine / BB / Fludrocortisone / SSRI (Fluoxetine; Paroxetine; Venlafaxine); consider DDD pacemaker in the case of refractory syncope with dominant cardioinhibitory response (no benefit in ★ VPS-II; positive results in ★ ISSUE-3)



CAROTID SINUS HYPERSENSITIVITY

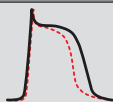
CAROTID SINUS MASSAGE: Apply pressure with 2 fingers (circular movements) for 10 s over the carotid pulse (at the level of the cricoid cartilage) with cardiac monitor

- **Contraindications:** carotid murmur; history of TIA - stroke
- **Cardioinhibitory response:** ventricular asystole > 3 s during massage → indication for DDD or VVI pacemaker in a patient with syncope

6.8/ ANTIARRHYTHMIC DRUGS (AAD)

VAUGHAN WILLIAMS CLASSIFICATION		
CLASS IA - SODIUM CHANNEL BLOCKING AGENTS		
	<ul style="list-style-type: none"> • Slow phase 0 (↘ conduction velocity) • Prolong the duration of the action potential (↗ QT) • Intermediate kinetics • Act on atria / ventricles / accessory pathway 	
Quinidine	<ul style="list-style-type: none"> • Indications: Atrial and ventricular arrhythmias; Brugada; short QT syndrome; Idiopathic VF • Dose: 6 to 10 mg/kg IV (0.3-0.5 mg/kg/min); 300 to 600 mg PO qid 	<ul style="list-style-type: none"> • ↗ QRS (avoid ↗ > 25 %) • ↗ QT (TdP) • Hypotension; Nausea; Vomiting; Diarrhea; Thrombocytopenia; Lupus; Fever; Arrhythmogenic
Procainamide	<ul style="list-style-type: none"> • Indications: Atrial and ventricular arrhythmias; CCV AF (combined with AV node blocking agent); Pre-excited AF • Dose: 15-20 mg/kg IV x 60 min (max 1 g) then 2 to 6 mg/min IV; stop if hypotension / ↗ QRS > 50% / arrhythmia controlled 	<ul style="list-style-type: none"> • Metabolite: N-acetylprocainamide (class III effect; renal elimination) • Adverse effects: ANA+; drug Lupus; Arrhythmogenic; Infra-His block; ↗ QT (torsade de pointes); Negative inotropic agent with high-dose; Hypotension
Disopyramide	<ul style="list-style-type: none"> • Indications: Atrial and ventricular arrhythmias; HCM • Dose: 100-300 mg PO tid to qid 	<ul style="list-style-type: none"> • Negative inotropic agent • Vagolytic effect (↗ heart rate) • Urinary retention; constipation; ↗ QT (TdP)

CLASS IB – SODIUM CHANNEL BLOCKING AGENTS



- Decrease the duration of the action potential
- Rapid kinetics
- Main effect: ventricular

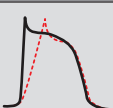
Lidocaine

- **Indications:** Ventricular arrhythmias; (enhanced effect in ischemic tissues)
- **Dose:** 1 to 3 mg/kg IV (20-50 mg/min) then 1-4 mg/min (dilution: 2 g / 500 mL D5%)
- CNS toxicity (faintness; paresthesia; confusion)

Mexiletine

- **Indications:** Ventricular arrhythmias; long QT syndrome 3
- **Dose:** 150 to 300 mg PO bid to tid
- Sinus bradycardia; hypotension
- CNS toxicity (dysarthria; faintness; paresthesia; confusion)

CLASS IC – SODIUM CHANNEL BLOCKING AGENTS



- Slow phase 0 (↘ conduction velocity)
- Slow kinetics
- **Use-dependent effect:** maximum antiarrhythmic effect at high HR (receptor open or inactivated)
- ↗ **QRS duration** (avoid ↗ > 25 %) especially at high HR

Flecainide

- **Indications:** AF; Flutter; PSVT; catecholaminergic polymorphic VT
- **Dose:** 50 to 200 mg bid (combine with AV node blocking agent)
- Avoid in patients with CAD (★ CAST) / LV dysfunction
- Risk of organization of AF into flutter with 1:1 AV conduction
- Negative inotropic agent
- ↗ pacemaker stimulation threshold

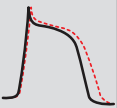
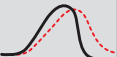
Propafenone

- **Indications:** AF; Flutter; PSVT
- **Dose:** 150 to 300 mg PO bid to tid (in combination with AV node blocking agent)
- Avoid in CAD / LV dysfunction
- Hepatic metabolism (7% of patients are slow metabolizers)
- Negative inotropic agent
- ↗ pacemaker stimulation threshold

CLASS II – BETA-BLOCKERS

Beta-blockers

- Block beta-adrenergic receptors
- **Indications:** supraventricular and ventricular arrhythmias
- **Metoprolol:** 2.5 to 5 mg IV every 5 min x 3
- **Esmolol:** 0.5 kg /mg IV bolus then 50-200 µg/kg/min (dilution: 2500 mg/250 mL)
- **Adverse effects:** Negative inotropic agent; bronchospasm; hypotension; bradycardia; block; rebound effect on discontinuation; depression; exacerbation of severe PAD; masking of hypoglycemia symptoms; nightmares; erectile dysfunction

CLASS III – POTASSIUM CHANNEL BLOCKING AGENTS		
	<ul style="list-style-type: none"> • Increase the duration of the action potential; minimal effect on phase 0 • ↗ QT interval (risk of TdP) 	
Amiodarone	<ul style="list-style-type: none"> • Indications: AF; Flutter; VT; VF; PSVT • Dose: 150 mg IV x 10 min then 1 mg/min IV x 6 h then 0.5-1 mg/min thereafter (dilution: 450 mg/250 mL D5%) • PO: 800 to 1600 mg PO daily x 7-14 days (10 g) then 100 to 600 mg daily • Adverse effects: ►► Amiodarone 	
Sotalol	<ul style="list-style-type: none"> • Indications: AF; PSVT; ventricular arrhythmias • Dose: 80 to 160 mg bid 	<ul style="list-style-type: none"> • ↗ QT (TdP) • Inverse use-dependent: maximum antiarrhythmic effect at lower HR (resting receptors); ↗ QT at low HR • ★ SWORD: ↗ mortality post-myocardial infarction with LVEF ≤ 40% with d-Sotalol (without BB effect) • Renal excretion
Dronedarone	<ul style="list-style-type: none"> • Indications: Paroxysmal AF (★ ATHENA) • Dose: 400 mg bid 	<ul style="list-style-type: none"> • Contraindication: NYHA III-IV heart failure (★ ANDROMEDA); permanent AF (★ PALLAS); liver disease
Dofetilide	<ul style="list-style-type: none"> • Indications: AF and Flutter • Dose: 0.125 to 0.5 mg PO bid 	<ul style="list-style-type: none"> • ↗ QT (initiate in hospital; avoid if baseline QTc ≥ 440 ms) • Renal excretion • Safe in CAD or LV dysfunction (★ DIAMOND)
Ibutilide	<ul style="list-style-type: none"> • Indications: CCV of AF and Flutter (success: 70%) • Dose: 1 mg x 10 min (with MgSO₄; repeat x 1 PRN) 	<ul style="list-style-type: none"> • ↗ QT - TdP; Monitoring x 8 h post-dose • Contraindicated if QTc > 440 ms or hypokalemia
CLASS IV – CALCIUM CHANNEL BLOCKING AGENTS		
	<ul style="list-style-type: none"> • Decrease conduction velocity (phase 0) of SA and AV nodes 	
Verapamil and Diltiazem	<ul style="list-style-type: none"> • Indications: PSVT; AF Flutter (rate control); fascicular VT • Diltiazem: 0.25 mg/kg IV x 2 min (2nd bolus after 15 min); 120-360 mg PO daily 	<ul style="list-style-type: none"> • Negative inotropic agent (avoid in the presence of LV dysfunction) • Hypotension; Bradycardia; Leg edema; Drug interactions

OTHER AAD		
Digoxin	<ul style="list-style-type: none"> ↗ Vagal tone Indications: Rate control of HR in AF (at rest) Dose: loading dose of 0.5 to 1 mg x 24 h (PO or IV) then 0.0625 to 0.25 mg PO daily 	<ul style="list-style-type: none"> Toxicity: calcium overload → delayed afterdepolarization / ↗ automaticity ▶▶ Chapter 9 - Digoxin poisoning Renal excretion
Adenosine	<ul style="list-style-type: none"> Brief inhibition of AV conduction Indications: PSVT; VT RVOT Dose: Adenosine: 6 to 12 mg rapid IV 	<ul style="list-style-type: none"> Adverse effects: precipitates AF (1-15%); flushing; dyspnea; retrosternal chest pain Contraindications: asthma; theophylline Transplant recipient or Dipyridamole: use a dose of 3 mg
Atropine	<ul style="list-style-type: none"> Vagolytic Indications: symptomatic bradycardia Dose: 0.5 to 1 mg IV (up to 2 mg) 	

6.9/ AMIODARONE

ADVERSE EFFECTS

Pulmonary toxicity (2%)	Toxicity correlated with cumulative dose <ul style="list-style-type: none"> Interstitial lung disease; Organizing pneumonia / BOOP; ARDS Cough; Dyspnea; Fever PFT: ↘ DLCO / restrictive pattern HDCT: Interstitial / alveolar opacities; Ground glass; Fibrosis Diagnosis of exclusion (rule out infection and heart failure) 	<ul style="list-style-type: none"> Permanently discontinue Amiodarone Corticosteroids if severe Slow improvement (long half-life of amiodarone)
GI toxicity (30%)	<ul style="list-style-type: none"> Nausea; Anorexia; Constipation ↗ AST ALT 2 x ULN Symptomatic hepatitis (3%) - Cirrhosis 	<ul style="list-style-type: none"> Rule out DDx Consider discontinuation
Hypothyroidism (20%)	<ul style="list-style-type: none"> ↗ TSH and ↘ Free T4 Risk factors: Female; underlying autoimmune thyroid disease (positive antibody); failure to escape from the Wolff-Chaikoff effect 	<ul style="list-style-type: none"> L-Thyroxine Continue Amiodarone
Hyperthyroidism (10 %)	<ul style="list-style-type: none"> ↘ TSH and ↗ Free T4 ↗ INR if treated with warfarin Thyroid scintigraphy falsified by the iodine load of Amiodarone Etiologies <ol style="list-style-type: none"> T4 synthesis: Underlying thyroid disease (Graves; multinodular goiter) exacerbated by iodine load T4 release: Destructive thyroiditis (fever; painful gland); hypothyroid phase several weeks or months later Mixed (majority) 	According to etiology <ol style="list-style-type: none"> PTU or Methimazole; Discontinue Amiodarone once hyperthyroid symptoms have been controlled (as Amiodarone blocks conversion of T4→T3) Prednisone; ± Discontinue Amiodarone Corticosteroids + antithyroid drugs (then stop antithyroid drugs if good response to corticosteroids in ≤ 1 week of treatment)

Skin	<ul style="list-style-type: none"> • Photosensitivity (up to 75%) • Blue discolouration (< 10%) 	• Avoid exposure to sunlight
CNS	Ataxia; Paresthesia; Polyneuritis; Tremor	Dose-dependent effect
Ophtalmic	Halo; Optic neuropathy; Photophobia; Blurred vision; Corneal microdeposits	Discontinue Amiodarone in the presence of optic neuropathy
Cardiac	Bradycardia; Block; Arrhythmogenic (< 1%); ↗ defibrillation threshold ; ↘ tachycardia CL	

MAJOR DRUG INTERACTIONS: Digoxin; Procainamide; Disopyramide; Diltiazem; Flecainide; Phenytoin; Cyclosporine; Simvastatin; Atorvastatin

➤ **Warfarin:** it is recommended to decrease the dose of warfarin by 30-50% on initiation of Amiodarone

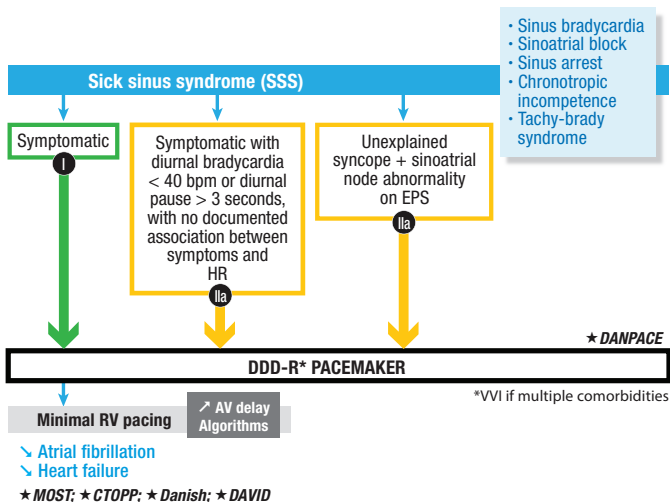
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WORK-UP BEFORE STARTING AMIODARONE: TSH - Free T4 - T3; LFTs; CXR; Ophthalmological examination if underlying abnormalities; renal function; ECG

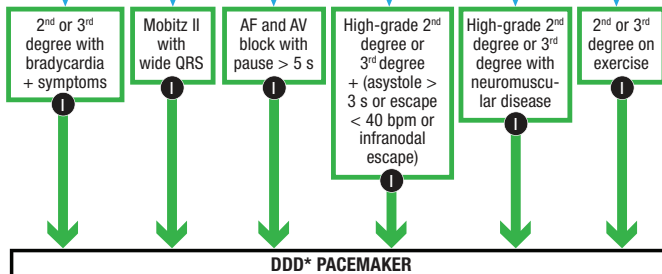
FOLLOW-UP ANALYSES: TSH - Free T4 every 6 months; AST / ALT every 6 months; annual CXR

6.10/ PERMANENT PACEMAKER (PPM)

INDICATIONS



AV node disease - AV block



*VI if permanent AF

* VI as alternative if multiple comorbidities

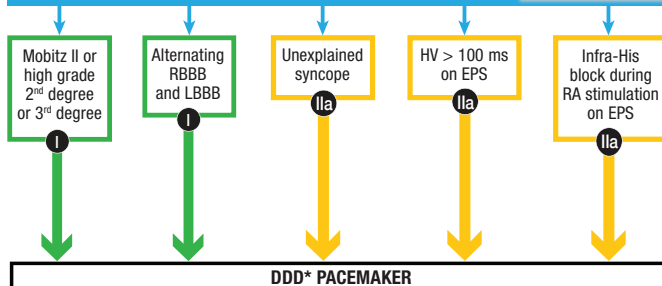
* CRT if LVEF < 35% and %V-Pace > 40%

* Consider VDD if normal sinoatrial node



AV node disease - Bifascicular block

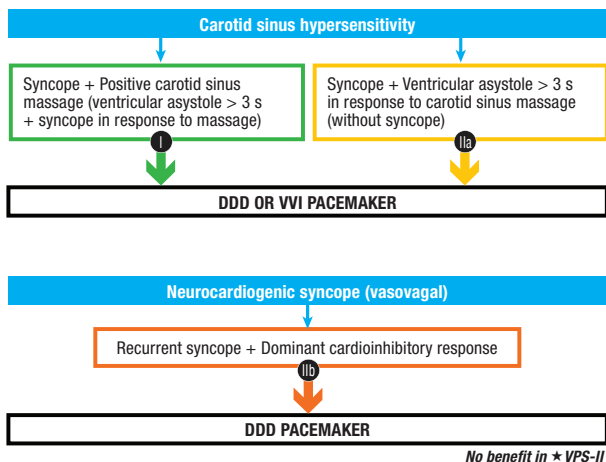
- RBBB + LAHB
- RBBB + LPHB
- LBBB



* VI if permanent AF

* VI as alternative if multiple comorbidities

* CRT if LVEF < 35% and %V-Pace > 40%



TYPES OF PERMANENT PACEMAKERS

NBG CODE				
-1- Chamber paced	-2- Chamber sensed	-3- Response to sensing	-4- Rate modulation	-5- Multisite pacing
<ul style="list-style-type: none"> • O = None • A = Atrium • V = Ventricle • D = Dual (A + V) 	<ul style="list-style-type: none"> • O = None • A = Atrium • V = Ventricle • D = Dual (A + V) 	<ul style="list-style-type: none"> • O = None • T = Triggered • I = Inhibited • D = Dual (T + I) 	<ul style="list-style-type: none"> • O = None • R = Rate modulation 	<ul style="list-style-type: none"> • A = Atrium • V = Ventricle • D = Dual (A + V)

AAI: atrial pacing at the lower rate limit in the absence of sensing of an atrial event; indicated in sick sinus syndrome with preserved AV conduction

VVI: ventricular pacing at the lower rate limit in the absence of sensing of a ventricular event; absence of atrioventricular synchrony; indicated in AV block with permanent AF

DDD: atrial and ventricular pacing; atrial and ventricular sensing; indicated in AV block

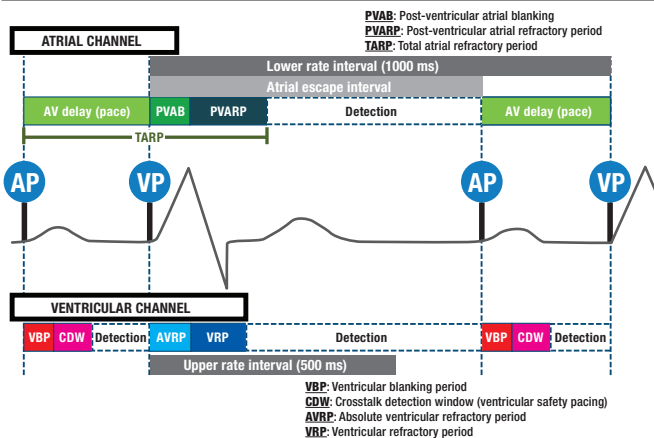
- **4 possibilities:** **A)** A-Sense / V-Sense; **B)** A-Sense / V-Pace (at the end of the AV interval in the absence of sensing of a ventricular event); **C)** A-Pace / V-sense (A-Pace at the end of the atrial escape interval in the absence of sensing of an atrial event); **D)** A-Pace / V-Pace
- **AV delay:** set a long AV delay (not exceeding 250-300 ms) to promote intrinsic AV conduction and minimize ventricular pacing
 - **A-Pace / V-Pace delay > A-Sense / V-Pace delay** (A-Sense: part of the atrium is already + depolarized)

V00: asynchronous ventricular pacing; mode used in pacemaker-dependent patients submitted to a source of electromagnetic interference (e.g.: electrocautery)

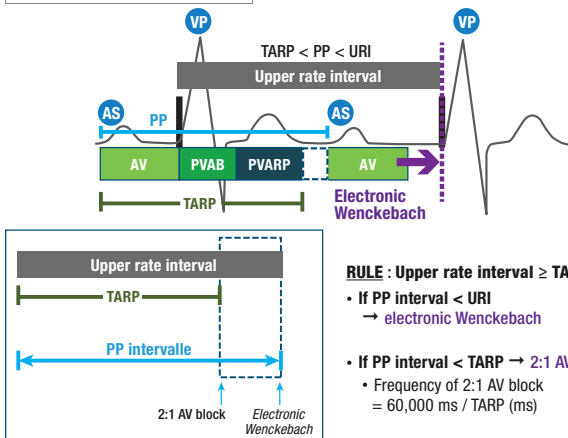
VDD: ventricular pacing with preserved atrioventricular synchrony on sensing of intrinsic P waves; requires a single lead (proximal atrial sensing by a ring; bipolar distal ventricular lead); consider in AV block in the absence of sick sinus syndrome

DDI: absence of “tracking” of sensed atrial events; V-Pace when the “lower rate interval” is reached (and A-Pace when the atrial escape interval is reached in the absence of a sensed event); indicated for atrial tachyarrhythmia with ineffective “mode-switch”

DDD PACEMAKER INTERVALS



MAXIMUM VENTRICULAR PACING RATE



RULE: Upper rate interval \geq TARP

- If PP interval $<$ URI \rightarrow **electronic Wenckebach**
- If PP interval $<$ TARP \rightarrow **2:1 AV block**
 - Frequency of 2:1 AV block = $60,000 \text{ ms} / \text{TARP (ms)}$

SPECIAL FUNCTIONS / ALGORITHMS

RATE ADAPTIVE: DDD-R or AAI-R or VI-R; increased pacing rate when the patient is active (via activity sensor); activate in the case of symptomatic chronotropic incompetence / sick sinus syndrome

HYSTERESIS: lower rate interval following V-Sense longer than lower rate interval following V-Pace (e.g.: 50 bpm vs 70 bpm); promotes intrinsic rhythm

AAI ↔ DDD MODE (MVP MODE): AAI mode switches to DDD mode when ≥ 2 of the previous 4 A-A intervals do not contain V-Sense

DYNAMIC AV DELAY: AV delay decreases at higher HR (= \searrow TARP); useful in patients with AV block and risk of 2:1 block on exercise

MODE SWITCH: DDD mode switches to DDI mode following atrial tachyarrhythmia to prevent tracking of this tachyarrhythmia

VENTRICULAR SAFETY PACING: following A-Pace → early ventricular pacing (AV delay: 100 ms) in the presence of a ventricular event detected inside the cross-talk detection window (preventing asystole in the presence of cross-talk or preventing R on T in the presence of a PVC)

POST-PVC EXTENSION OF PVARP: extension to 400 ms; prevents detection of a post-PVC retrograde P wave and therefore **the development of PMT**

RATE SMOOTHING: prevents an abrupt change of HR (during paroxysmal sinus arrest or following a mode switch)

RATE DROP RESPONSE: pacing at a higher rate (100-120 bpm) following an abrupt drop in HR (due to neurocardiogenic syncope)

NOISE RESPONSE: VOO or DOO mode activated following noise (nonphysiological signals)

PACEMAKER MONITORING

Battery	<ul style="list-style-type: none"> • \searrow Voltage and \nearrow Impedance with time • ERI: Elective replacement indicator (< 3 months)
Lead	<ul style="list-style-type: none"> • Impedance: significant change > 200 ohms • Low impedance (< 250 Ohms): insulation defect • Increased impedance (> 1000 Ohms): short circuit (lead fracture; loose set screw) • Chest x-ray PRN
Events	<ul style="list-style-type: none"> • % A-Pace; % V-Pace; Frequency histogram • Saved episodes; AT/AF; Mode switch; Ventricular high rate; PMT
Sensitivity	<ul style="list-style-type: none"> • Atrial: from 0.3 to 0.6 mV • Ventricular: from 2 to 3.5 mV
Pacing	<ul style="list-style-type: none"> • Safety margin: programmed amplitude → twice the pacing threshold (or automatic capture) • Pulse width: 0.4 to 0.5 ms

MINIMUM FOLLOW-UP FREQUENCY FOR PPM, CRT, OR ICD

Post-implantation follow-up	<ul style="list-style-type: none"> • < 72 h post-implant (in person) • 2 to 12 weeks post-implant (in person)
PPM or CRT follow-up	<ul style="list-style-type: none"> • 3 to 12 months (in person or by remote monitoring) • At least once a year in person
ICD follow-up	<ul style="list-style-type: none"> • 3 to 6 months (in person or by remote monitoring) • At least once a year in person
Signs of battery depletion	<ul style="list-style-type: none"> • Every 1 to 3 months (in person or by remote monitoring)

PACEMAKER DYSFUNCTION

Capture failure	<ul style="list-style-type: none"> • Early post-implant: lead migration; myocardial perforation; maturation (inflammatory reaction) • Late lead maturation: exit block • Modified threshold: myocardial infarction; cardiomyopathy; acidosis; electrolyte disorders; drugs (class IC AAD; Sotalol) • Ineffective autocapture algorithm • Inadequate programming: insufficient pacing amplitude safety margin • Lead: insulation defect; lead fracture; loose set screw • Battery depletion • Failure to capture: pacing during the refractory period; \pm associated undersensing
Output failure	<ul style="list-style-type: none"> • Oversensing (inhibition) • Lead: insulation defect; short circuit (lead fracture; loose set screw) • Hysteresis • Battery depletion • Post-PVC extension of PVARP • Generator dysfunction (rare)
Undersensing	<ul style="list-style-type: none"> • Inadequate intrinsic signal: PVC or APC • Signal modification: myocardial infarction; cardiomyopathy; conduction disorder; metabolic disorder • Programming: high sensitivity • Lead: migration; maturation; insulation defect; lead fracture; loose set screw • Magnet • Noise response • Safety pacing function • Battery depletion • Pseudofusion • Functional undersensing (refractory period)
Oversensing	<ul style="list-style-type: none"> • Cross-talk: pacing of one chamber induces sensing of an event in the other chamber; minimized by blanking • Far-field: QRS detected as atrial event • Oversensing of T wave • Electromagnetic interference: electrocautery; MRI • Myopotentials (unipolar electrode) • Lead: insulation defect (internal contact of the two conductors); short circuit (lead fracture; loose set screw)

Pacing at a rate different from programmed rate	High heart rate <ul style="list-style-type: none"> • Rate-adaptive: R • Undersensing • Tracking of intrinsic atrial rhythm (or atrial oversensing) • Rate smoothing • Rate drop • Pacemaker-mediated tachycardia • Runaway pacemaker (battery depletion) 	Low heart rate <ul style="list-style-type: none"> • Oversensing • Hysteresis • AAI ↔ DDD • Sleep mode • Battery depletion
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PACEMAKER-MEDIATED TACHYCARDIA (PMT)

- **Risk factors:** **A)** PVC with retrograde conduction; **B)** Atrial capture failure; **C)** Very long programmed AV delay; **D)** Atrial oversensing or undersensing
- **Mechanism:** Retrograde V-A conduction (often post-PVC) → A-Sense (outside of the PVARP) → V-Pace → retrograde V-A conduction → A-Sense (and so on)
- **Diagnosis:** **A)** A-Sense / V-Pace at the maximum pacing rate; **B)** A-Sense following V-Pace with V-A interval < 400 ms; **C)** Discordance between pacing rate and activity sensor; **D)** Modulation of P-V period
- **Prevention / Termination:** **A)** PVARP > retrograde V-A conduction time (while avoiding excessively prolonged TARP, which would lead to low frequency 2:1 block); **B)** Extension of post-PVC PVARP; **C)** 1 cycle without V-Pace following A-Sense during PMT

PACEMAKER SYNDROME: secondary to loss of AV synchrony (± atrial contraction on closed AV valve) with VVI pacemaker; tiredness / retrosternal chest pain / dyspnea / cough / confusion / faintness / syncope

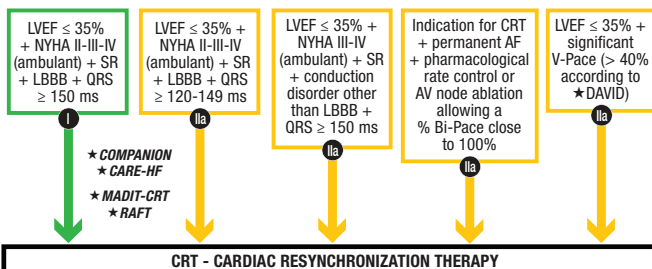
DIAPHRAGMATIC STIMULATION: lead close to phrenic nerve; incorrectly positioned lead (cardiac vein; myocardium perforation; migration); high stimulation amplitude

6.11/ CARDIAC RESYNCHRONIZATION THERAPY (CRT)

HEART FAILURE: altered electromechanical coupling → inter- and intraventricular delays → ventricular asynchrony → ↗ systolic dysfunction → altered myocardial metabolism / functional MR / ventricular remodeling / LV dilatation

SCIENTIFIC EVIDENCE	
<ul style="list-style-type: none"> • ★ COMPANION: LVEF ≤ 35% + NYHA III or IV (ambulant) + SR + QRS ≥ 120 ms + Hospitalization for heart failure during the previous year • ★ CARE-HF: LVEF ≤ 35% + NYHA III or IV (ambulant) + SR + QRS ≥ 150 ms (120-149 ms with TTE criteria of asynchrony) 	<ul style="list-style-type: none"> • ★ MADIT-CRT: LVEF ≤ 30% + NYHA I (15%) or NYHA II (85%) + SR + QRS ≥ 130 ms • ★ RAFT: LVEF ≤ 30% + NYHA II (80%) or NYHA III (20%) + QRS ≥ 130 ms
<ul style="list-style-type: none"> • ↘ All-cause mortality • ↘ Hospitalization • Improvement of quality of life • Reverse remodeling 	<ul style="list-style-type: none"> • ↘ All-cause mortality (★ RAFT) • ↘ Hospitalization • Improvement of quality of life • Reverse remodeling
MAINLY BENEFICIAL IN LBBB WITH QRS ≥ 150 MSEC	

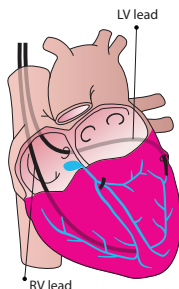
INDICATIONS



* Life expectancy with satisfactory functional capacity > 1 year

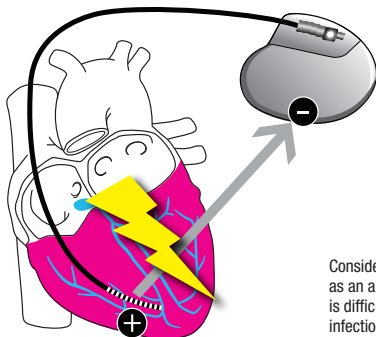
PROGRAMMING

RA pacing	<ul style="list-style-type: none"> • Minimal to avoid interatrial asynchrony • Minimum rate: 50 bpm • Do not activate "R"
AV delay	<ul style="list-style-type: none"> • 100-120 ms (minimize intrinsic AV conduction; ensure adequate duration of atrial kick) • Consider echocardiography-guided optimization in the presence of a pseudonormal (grade II) or restrictive (grade III) mitral diastolic pattern
LV lead position	<ul style="list-style-type: none"> • Basal posterolateral wall (site of maximum electromechanical delay) • Avoid scars whenever possible (LGE on MRI); target adequate threshold; avoid phrenic nerve stimulation (electronic reprogramming of vectorial stimulation configuration PRN)
V-V delay	<ul style="list-style-type: none"> • Simultaneous or pre-excitation of LV stimulation (30 ms) • Echocardiographic optimization PRN in non-responders (using aortic VTI and/or deformation imaging and/or RV - LV pre-ejection intervals)
Maximize Bi-Pace	<ul style="list-style-type: none"> • Target Bi-Pace $> 98\%$ • AF \rightarrow AV node blocking agent or RF ablation of AV node • Frequent PVCs \rightarrow AAD or RF ablation
ECG	<ul style="list-style-type: none"> • V1: dominant R wave • I: negative • V4-V5: positive in the case of basal LV stimulation (negative if apical) • Frontal axis: -90° to 180°



V1	I	FRONTAL AXIS
RV apical stimulation		0 to -90°
Resynchronization therapy		-90 to 180°

6.12/ IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR (ICD)



Consider **subcutaneous defibrillator** as an alternative when venous access is difficult; after removal of an ICD for infection; in young patients

SCIENTIFIC EVIDENCE

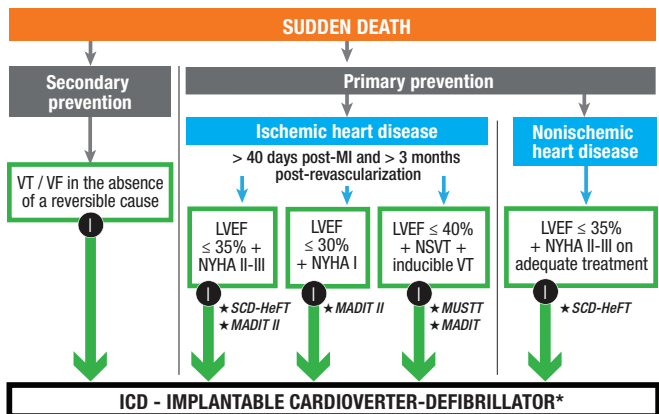
SECONDARY PREVENTION: ★ AVID; ★ CIDS; ★ CASH

- Reduction of the absolute mortality (vs Amiodarone): 10.5% at 36 months (NNT 10 patients) +

PRIMARY PREVENTION: reduction of absolute mortality of 5-8% at 36 months (NNT 14-18 patients) +

- ★ **MADIT-I**: Ischemic heart disease; LVEF ≤ 35%; NYHA I-II-III, NSVT; inducible VT
→ ↘ all-cause mortality
- ★ **MUSTT**: Ischemic heart disease; LVEF ≤ 40%; NYHA I-II-III, NSVT; inducible VT
→ ↘ all-cause mortality
- ★ **MADIT-II**: Ischemic heart disease; LVEF ≤ 30%; NYHA I-II-III → ↘ all-cause mortality
- ★ **DEFINITE**: Nonischemic heart disease; LVEF ≤ 35%; NYHA I-II-III, NSVT (or ≥ 10 PVCs / h)
→ trend to ↘ all-cause mortality
- ★ **SCD-HeFT**: LVEF ≤ 35%; (ischemic or nonischemic heart disease); NYHA II-III
→ ↘ all-cause mortality
- ★ **DINAMIT**: LVEF ≤ 35%; < 40 days post-MI; decreased HR variability or high resting HR
→ no benefit
- ★ **IRIS**: LVEF < 40%; < 30 days post-MI; HR > 90 bpm or NSVT > 150 bpm → no benefit

INDICATIONS



PROGRAMMING – SECONDARY PREVENTION

DETECTION DURATION: ≥ 30 intervals (≥ 6 –12 sec)

SLOWEST ZONE: at least 10 bpm below the documented tachycardia rate (but not faster than 200 bpm except for some young patients) \rightarrow ATP (≥ 1 burst attempt - 8 impulses at 88% of VT CL; 10 ms scan decrement) \rightarrow Shock

VF: > 250 bpm \rightarrow ATP while charging \rightarrow Shock (full output)

MANAGEMENT FOLLOWING AN ICD SHOCK

MEDICAL ASSESSMENT: < 24 h (urgent if multiple shocks or symptoms)

APPROPRIATE SHOCK: VF; monomorphic VT; polymorphic VT

INAPPROPRIATE SHOCK: apply a magnet over the device; reprogram treatment / parameters

- **Supraventricular tachycardia** \rightarrow modify therapy zones; optimize discriminator programming; AV node blocking agent / AAD; RF ablation
- **T wave oversensing (and small R wave)** \rightarrow decrease ventricular sensitivity (however, must be sufficient to detect VF; defibrillator test PRN); prolong the ventricular refractory period; modify sensing decay; lead repositioning
- **Atrial far-field** (distal coil of an integrated bipolar electrode close to the tricuspid valve)
- **R-wave double counting** \rightarrow modify sensing decay; prolong the refractory period; decrease ventricular sensitivity (however, must be sufficient to detect VF; defibrillator test PRN)
- **Electromagnetic interference**
- **Myopotentials**
- **Lead** (insulation defect; lead fracture; loose set screw)

ELECTRICAL STORM: \gg Ventricular fibrillation

PREVENTION OF NEW SHOCKS: BB; Amiodarone; Sotalol; therapy reprogramming; RF ablation

SHOCK APPROPRIATE BUT INEFFECTIVE

- **Increased defibrillation threshold:** ischemia; progressive heart failure; AAD (sodium channel blocking agents; Amiodarone); electrolyte / metabolic disorders; pleural / pericardial effusion
- **Secondary to defibrillator:** insufficient programmed shock amplitude; battery depletion; lead (insulation defect; lead fracture; loose set screw; migration)

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Adult congenital heart disease & Heart disease in pregnant women

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7.1/ SEGMENTAL ASSESSMENT & FETAL CIRCULATION

SEGMENTAL ASSESSMENT

POSITION OF THE APEX: **A) Levocardia** (apex points to the left); **B) Dextrocardia** (apex points to the right); **C) Mesocardia** (apex in the middle)

ATRIAL SITUS (solitus; inversus; ambiguus): according to the position of the atrial appendages, IVC (which drains into the RA) and visceral situs

- **Right atrial appendage morphology:** large base, triangular shape, contains numerous pectinate muscles
- **Left atrial appendage morphology:** narrow base, finger-shaped

AV CONNECTION: **A)** Concordance: morphological LA connected to morphological LV (and RA connected to RV); **B)** Discordance

- **Right ventricle morphology:** moderator band, extensive trabeculations, infundibulum, tricuspid valve
 - **Tricuspid valve:** 3 leaflets - septal attachments - closer to apex than M valve - absence of distinct papillary muscles
- **Left ventricle morphology:** fine trabeculations; mitral valve
 - **Mitral valve:** 2 leaflets - mitro-aortic continuity - 2 papillary muscles - less apical than the T valve

VENTRICULO-ARTERIAL CONNECTION: **A)** Concordance: Morphological LV connected to the aorta; morphological RV connected to the PA; **B)** Discordance; **C)** Double-outlet (> 50% of the aorta and PA arise from the same ventricle)

- **Aorta:** "Candy cane"; 3 vessels (innominate artery, left carotid artery, left subclavian artery); always associated with its aortic valve
- **Pulmonary trunk:** rapidly divides into RPA and LPA; always associated with its pulmonary valve

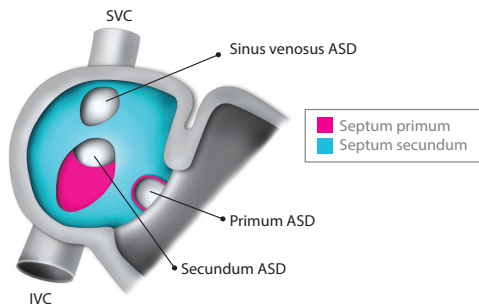
FETAL CIRCULATION

1. **DUCTUS VENOSUS:** allows oxygenated umbilical blood to short-circuit the liver and reach the IVC
2. **FORAMEN OVALE:** allows blood derived from the IVC (part of which is derived from the placenta and is oxygenated) to go directly to the left heart (preferentially perfusing the coronary arteries and CNS)
3. **PATENT DUCTUS ARTERIOSUS:** allows blood (predominantly derived from the SVC) to go from the right heart to the descending aorta (to the placenta)

7.2/ ATRIAL SEPTAL DEFECT (ASD)

4 TYPES

1. **SECUNDUM ASD (80 %):** in the fossa ovale
2. **PRIMUM ASD (15 %):** close to AV valves; associated with AV canal defect
3. **SINUS VENOSUS ASD (5 %):** close to the origin of the SVC (exceptionally IVC); associated with anomalous pulmonary venous connection (R > L)
4. **CORONARY SINUS ASD (1 %):** communication between the coronary sinus and the LA; associated with persistent left SVC



SIGNIFICANT ASD: generally > 10 mm with $Q_p/Q_s > 1.5:1$

ACCENTUATION OF L \rightarrow R SHUNT: in the presence of \searrow LV compliance or \nearrow LA pressure (age; LVH; HTN; cardiomyopathy; myocardial infarction; MR...)

LUTEMBACHER SYNDROME: ASD + rheumatic MS

HOLT-ORAM SYNDROME: autosomal dominant; TBX5 mutation; abnormalities of hands; secundum ASD

FEATURES: left parasternal heave; palpable dilated PA (2nd left intercostal space); **fixed split S2**; pulmonary ejection murmur (\nearrow flow); tricuspid diastolic rumble in the presence of significant shunt; TR murmur in the presence of right heart failure

ECG

- \triangleright **Secundum ASD:** Incomplete RBBB; right axis deviation; RAH; Notch on R wave in inferior leads
- \triangleright **Primum ASD:** RBBB; left axis deviation; RAH
- \triangleright **Sinus venosus ASD:** non-sinus rhythm (negative P wave in inferior leads)

+

CXR: RA-RV dilatation; \nearrow vascularization; prominent central PA

TEE: evaluate pulmonary venous return; ASD dimensions; possibility of percutaneous closure; agitated-saline PRN (R \rightarrow L shunt = contrast in left chambers; L \rightarrow R shunt = negative contrast in right chambers)

COMPLICATIONS

- a) Right heart failure (\pm TR) (volume overload)
- b) Atrial arrhythmias: typical flutter; IART; AF; SSS after repair
- c) Paradoxical embolism
- d) PHT (5-9%) (rarely severe)

INDICATIONS FOR ASD CLOSURE

- a) Dilatation of right chambers (I;B)
- b) Paradoxical embolism (IIa;C)
- c) Platypnea-orthodeoxia (IIa;C)
- d) PHT with marked L \rightarrow R shunt $> 1.5:1$ or with significant reactivity to vasodilator (IIb;C)
- e) Do not close if **irreversible PHT** with $sPAP > 2/3$ SBP or $PVR > 2/3$ SVR (III;C)

PERCUTANEOUS CLOSURE: possible if **secundum ASD < 38 mm with adequate margins** +
(distance > 5 mm from AV valves, coronary sinus, origin of SVC / IVC and right pulmonary veins)
and with **normal pulmonary venous return**

- > ASA for 6 months after ASD closure; **complications** (1 %) → prosthesis embolization; erosion (atrial wall or Ao); thromboembolism; arrhythmia - AF; endocarditis; tamponade

PACEMAKER LEADS: risk of paradoxical embolism if ASD not repaired

PREGNANCY: generally well tolerated; risk of paradoxical embolism

7.3/ PATENT FORAMEN OVALE (PFO)

Absence of fusion of septum secundum and septum primum at birth

25% of adults

ASSOCIATION WITH CRYPTOGENIC STROKE: possibility of paradoxical embolism

- > **Risk factors:** PFO > 5 mm or spontaneous R→L shunt or atrial septal aneurysm or prominent Eustachian valve

DIAGNOSIS: TEE with bubbles: **bubbles in ≤ 3 beats in left chambers**; facilitated by Valsalva maneuver +

TREATMENT OF CRYPTOGENIC STROKE: highly controversial

- 1) First-line ASA; Warfarin if documented DVT (± closure of PFO)
- 2) If recurrence: anticoagulation vs percutaneous closure
 - No convincing evidence for the superiority of percutaneous closure versus medical treatment (equivocal results in ★ CLOSURE-I, ★ RESPECT and ★ PC)

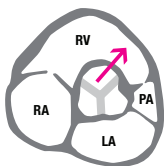
ANEURYSM OF INTERATRIAL SEPTUM: **redundant and mobile portion of the atrial septum with excursion ≥ 15 mm** from the midline +

7.4/ VENTRICULAR SEPTAL DEFECT (VSD)

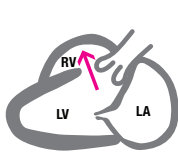
4 TYPES

- 1) **SUBARTERIAL** (5%): below the Ao and P valves; associated with AR (due to leaflet prolapse); numerous synonyms (outlet; conal; subpulmonary; subaortic; infundibular; supracristal)
- 2) **MEMBRANOUS** (80%): membranous septum; adjacent to Ao and T valves
- 3) **AV CANAL (INLET)**: below the AV valve (see AV canal defect)
- 4) **MUSCULAR** (15-20%): completely surrounded by muscle

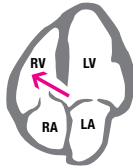
SUBARTERIAL VSD



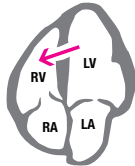
MEMBRANOUS VSD



INLET VSD



MUSCULAR VSD



CLINICAL FEATURES AND SEVERITY: Restrictive VSD (RV pressure \ll LV pressure) or nonrestrictive VSD (RV pressure similar to LV pressure)

- **Small VSD:** normal LV dimensions; absence of PHT; **holosystolic murmur in left parasternal region (3rd-4th left intercostal spaces) with spoke-wheel radiation \pm palpable thrill;** spontaneous closure is possible
- **Moderate VSD: LA and LV dilatation (volume overload);** PHT (reversible); \pm mitral diastolic rumble; S3; lateralized apex
- **Large VSD:** Progressive PHT then Eisenmenger; **absence of VSD murmur; signs of PHT (left parasternal heave; \nearrow and palpable P2; right S4; ejection click; Graham-Steel murmur and TR)**

COMPLICATIONS

- a) **Left heart failure (volume overload)**
- b) PHT (\pm right heart failure due to pressure overload)
- c) Progressive AR due to leaflet prolapse (subarterial VSD or membranous VSD)
- d) Double chamber RV (muscle band develops as a result of the VSD jet, inducing subpulmonary stenosis)
- e) Progressive subaortic stenosis
- f) Arrhythmia: AF; PVCs; NSVT; postoperative AV block
- g) Endocarditis

INDICATIONS FOR VSD CLOSURE

- a) **Significant VSD:** symptoms or progressive left ventricular dysfunction (volume overload) or right ventricular dysfunction (pressure overload) or $Q_p:Q_s > 2:1$ or $sPAP > 50$ mmHg (I;B)
- b) Subarterial or membranous VSD with **AR \geq moderate** (I;B)
- c) In the presence of **severe PHT** ($sPAP > 2/3$ SBP or $PVR > 2/3$ SVR), closure should only be considered in the case of $L \rightarrow R$ shunt $> 1.5:1$ or significant reactivity to vasodilators (I;B)
- d) **Double chamber RV:** significant obstruction (mean gradient > 40 mmHg or > 30 mmHg with symptoms)
- e) Endocarditis (IIa;B)

PERCUTANEOUS CLOSURE IS POSSIBLE: **A)** Trabecular muscle VSD situated away from T or Ao valves; **B)** Membranous VSD situated away from the Ao valve

PREGNANCY: a small VSD is well tolerated in the absence of associated PHT or LV dysfunction

7.5/ ATRIOVENTRICULAR CANAL DEFECT

Developmental anomaly of endocardial cushions

- a) **Partial atrioventricular canal defect:** intact interventricular septum; primum ASD; mitral cleft; AV valves inserted at same level (common annulus)
- b) **Complete atrioventricular canal defect:** defect of the septum on either side of the cardiac crux: non-restrictive VSD (inlet VSD) and primum ASD; common atrioventricular orifice (one common AV valve with 5 leaflets)
- **Associated Down syndrome** (Trisomy 21): small stature, typical facies, mental retardation, brachydactyly, atlanto-axial instability, hypothyroidism, propensity to PHT, OSAHS

ECG: Complete or incomplete RBBB; **left axis deviation; spontaneous or postoperative AV block;** atrial arrhythmia



VENTRICULOGRAPHY: Elongated LVOT (goose neck deformity)

COMPLICATIONS

- Left and right AV valve regurgitation**
- Left heart failure** (secondary to VSD and left AV valve regurgitation)
- Right heart failure** (secondary to ASD and right AV valve regurgitation)
- PHT; Eisenmenger if not operated
- Arrhythmias: AF; flutter; AV block**
- Progressive subaortic stenosis
- Paradoxical embolism
- Postoperative residual shunt
- Postoperative mitral stenosis

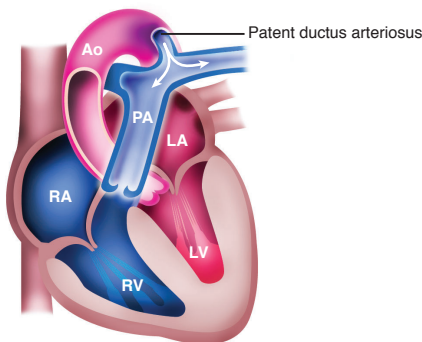
INDICATIONS FOR SURGERY

Patient already operated

- Hemodynamically significant** persistent or *de novo* defect (I;B)
- Deterioration of LV function** (I;B)
- Symptomatic left AV valve regurgitation** (I;B)
- Symptomatic left AV valve stenosis** (post-repair) (I;B)
- Subaortic obstruction** with mean gradient > 50 mmHg (I;B)
- Do not operate if **severe, irreversible PHT** (sPAP $> 2/3$ SBP or PVR $> 2/3$ SVR) (III;C)

7.6/ PATENT DUCTUS ARTERIOSUS

Connection between proximal pulmonary artery and descending aorta (distal to the left subclavian artery)



- SILENT DUCTUS ARTERIOSUS:** incidental finding on TTE
- SMALL PATENT DUCTUS ARTERIOSUS:** continuous murmur; minimal hemodynamic impact; $Qp/Qs < 1.5:1$
- MODERATE PATENT DUCTUS ARTERIOSUS:** continuous machinery murmur in 2nd left intercostal space \pm thrill; increased pulse pressure; bounding pulse; LV dilatation (lateralized, hyperdynamic apex); S3; reversible PHT (induces \searrow duration of the murmur)
- LARGE PATENT DUCTUS ARTERIOSUS:** Severe PHT; Eisenmenger physiology; absence of continuous murmur; **differential hypoxemia and cyanosis (lower limbs cyanosed; clubbing of the toes)** +

TTE: flow from aorta to PA visible on PLAX (RVOT/PA view); **diastolic flow reversal** in descending aorta

+

COMPLICATIONS

- Left heart failure (volume overload)**
- Progressive PHT
- Arrhythmias (AF)
- Endarteritis / Ductus aneurysm

INDICATIONS FOR SURGERY

- All cases of patent ductus arteriosus** except when silent or large with irreversible PHT (IIa;B)
- Endarteritis** (IIa;B)
- In the presence of **severe PHT** (sPAP > 2/3 SBP or PVR > 2/3 SVR), closure should only be considered in the case of L→R shunt > 1.5:1 or significant reactivity to vasodilators (IIa;B)

PERCUTANEOUS CLOSURE: preferable in the case of ductus arteriosus < 8 mm (without aneurysm) or in the presence of calcification

PREGNANCY: similar considerations to those of VSD

7.7/ LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

SUPRAVALVULAR AORTIC STENOSIS

Fixed obstruction above the sinus of Valsalva

CORONARY ARTERIES submitted to high pressures; risk of dilatation / ostial stenosis / early CAD; requires regular screening for CAD

WILLIAMS SYNDROME: autosomal dominant; 7q11.23 deletion; supravalvular aortic stenosis, peripheral pulmonary artery stenosis, renal artery stenosis, HTN, hypercalcemia, cognitive deficits, “cocktail” personality, elf-like facies

CLINICAL FEATURES: BP right arm >> BP left arm (Coanda effect with preferential jet to innominate artery); crescendo-decrescendo systolic murmur; suprasternal thrill; **increased A2:** absence of ejection click; S4; peripheral PA stenosis can cause end-systolic or continuous posterior murmur

+

VENTRICULOGRAPHY: “ballerina foot” pattern of LV

INDICATIONS FOR SURGERY (patch aortoplasty or ascending aorta replacement or resection with end-to-end anastomosis)

- Symptoms and/or mean gradient > 50 mmHg** (I;C)
- Doppler instantaneous maximum gradient > 70 mmHg** if mild obstruction (I;C)

VALVULAR AORTIC STENOSIS

BICUSPID AORTIC VALVE (▶▶| Chapter 4 - Valvular heart disease)

ASSOCIATED WITH: CoA; patent ductus arteriosus; ascending aortopathy

07

Adult congenital heart disease & heart disease in pregnant women

ROSS PROCEDURE: replace the aortic valve by the patient's pulmonary valve and replace the pulmonary valve by a cadaveric homologous graft; reimplantation of coronary arteries

- **Complications:** structural deterioration of the homologous P graft; aortopathy (specific to bicuspid aortic valve); AR; coronary stenosis

SUBVALVULAR AORTIC STENOSIS

Discrete membrane or tunnel-shaped LVOT stenosis

ASSOCIATED WITH: AR (valvular damage caused by the high velocity jet); VSD; AV canal defect; Shone complex

- **Shone complex:** multiple stenoses at different levels: **A)** Supravalvular mitral annulus or parachute mitral valve; **B)** Subvalvular aortic stenosis; **C)** Bicuspid aortic valve; **D)** CoA

DDX: HCM (absence of SAM in subaortic stenosis)

CLINICAL FEATURES: crescendo-decrescendo systolic murmur ± thrill; **no radiation to the carotids; absence of ejection click; AR diastolic murmur** +

INDICATIONS FOR SURGERY

- Symptoms with Doppler instantaneous maximum gradient > 50 mmHg** or mean gradient > 30 mmHg (I;C)
- Associated progressive AR** (I;C)

MEMBRANE: resection of the membrane ± myomectomy ± AVR

TUNNEL: Konno procedure (aortoventriculoplasty ± AVR)

- Complications: recurrence; AV block; iatrogenic VSD

7.8/ COARCTATION OF THE AORTA (COA)

Stenosis in the region of the ligamentum arteriosum (distal to the left subclavian artery)

ASSOCIATED ABNORMALITIES: Bicuspid aortic valve (80% of cases); aneurysm of the circle of Willis; collateral circulation (intercostal and mammary arteries); aortopathy; anomalous brachiocephalic circulation; aortic arch hypoplasia; VSD; Shone complex

- **Turner Syndrome** (45, X): CoA (35%); bicuspid aortic valve; ASD; VSD

SIGNIFICANT COA (IN THE ABSENCE OF COLLATERAL): HTN in arms with trans-CoA gradient on catheterization > 20 mmHg or with SBP in arms ≥ 20 mmHg higher than SBP in legs +

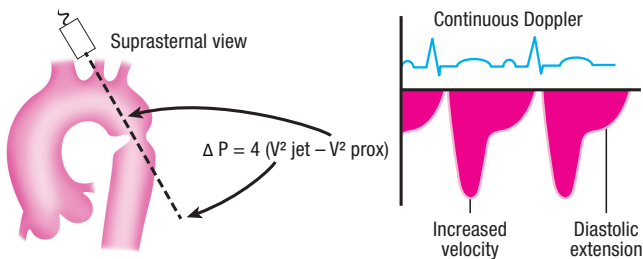
CLINICAL FEATURES

- **In the absence of collaterals:** HTN in arms; SBP in arms higher than in legs; radiofemoral delay on palpation of pulse; interscapular ejection murmur (rarely continuous); S₄; ⤴ A₂; systolic click / systolic murmur in the presence of bicuspid aortic valve
- **In the presence of collaterals:** continuous crescendo-decrescendo murmur in left parasternal region or left scapula

CXR: A) "3" sign: indentation of the aorta at the site of CoA with distal and proximal dilatation; **B) Erosion of the ribs:** intercostal collaterals +

TTE: turbulence and ⤴ velocity in descending Ao (suprasternal view) with diastolic extension of antegrade flow

- **Abdominal aorta:** ⤴ velocity of systolic flow and diastolic extension of antegrade flow



MANAGEMENT

- Congenital cardiology follow-up for life
- Control of BP (at rest and on exercise) and cardiovascular risk factors
- BB if aortopathy
- Imaging of the entire aorta (MRI) with regular follow-up (by TTE for ascending Ao / Ao valve and MRI for entire Ao)
- Brain MRI (rule out aneurysm of the circle of Willis)
- Avoid contact sports / isometric exercises if residual CoA or associated aortopathy

COMPLICATIONS

- Left heart failure (pressure overload)
- Persistent HTN
- Aortopathy / Aortic dissection
- Aortic valve disease
- Early CAD and PAD
- Intracranial aneurysms / Hemorrhage
- Endarteritis

INDICATIONS FOR SURGERY

- In the presence of significant CoA: peak-to-peak gradient ≥ 20 mmHg on catheterization or less in the presence of collaterals (I;C)

PERCUTANEOUS APPROACH (dilatation + stenting): preferable in the majority of cases (except in the case of a long or tortuous lesion) and preferred technique in the presence of re-coarctation

- Complications:** aortic dissection / rupture; stroke; aneurysm or pseudoaneurysm; aortobronchial fistula; re-CoA; persistent HTN

SURGICAL OPTIONS: resection with end-to-end anastomosis or graft placement; patch aortoplasty; subclavian flap aortoplasty; bypass graft

- Complications:** paraplegia; recurrent laryngeal nerve or phrenic nerve paralysis; dissection; aneurysm (post-patch aortoplasty); pseudoaneurysm; claudication of arms (subclavian flap aortoplasty); re-CoA; persistent HTN; endarteritis

POST-REPAIR FOLLOW-UP: Regular MRI and regular TTE

- Consider screening for intracranial aneurysms in the circle of Willis

PREGNANCY: pregnancy contraindicated if CoA not repaired (risk of IUGR - fetal loss - HTN); imaging of the entire Ao is necessary

7.9/ RIGHT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

SEVERITY

	MILD	MODERATE	SEVERE
Doppler instantaneous maximum gradient (mmHg)	< 36	36 - 64	> 64
Peak velocity (m/s)	< 3	3 - 4	> 4

* Doppler measurements not valid in the presence of long stenosis / tunnel stenosis

SUPRAVALVULAR PULMONARY STENOSIS / PERIPHERAL PULMONARY ARTERY STENOSIS

ASSOCIATED WITH: TOF; Williams syndrome; Noonan syndrome; Alagille syndrome; VSD; Congenital rubella

CLINICAL FEATURES: systolic ejection murmur (left parasternal region and posterior; increased by inspiration; sometimes continuous in peripheral pulmonary artery stenosis); absence of ejection click; increased or preserved P2; left parasternal heave

SUBVALVULAR PULMONARY STENOSIS

Associated with VSD or TOF

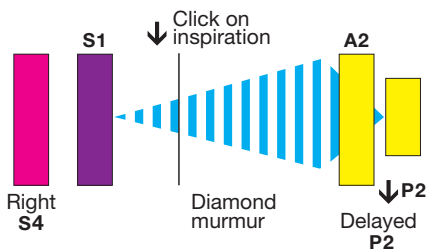
DOUBLE CHAMBER RV: mid-chamber obstruction secondary to a prominent muscle band; associated with VSD

VALVULAR PULMONARY STENOSIS

2 TYPES

- 1) Dome-shaped:** thin, pliable, mobile valve; fusion of commissures; post-stenotic dilatation of the PA
- 2) Dysplastic (10-15%):** thickened, immobile leaflets; associated with Noonan syndrome; absence of post-stenotic dilatation

CLINICAL FEATURES: Prominent a wave in jugular vein; left parasternal heave; crescendo-decrescendo systolic murmur ± thrill; **ejection click if the valve is pliable** (early if severe PS; absent in the presence of a dysplastic valve; **↘ during inspiration** due to premature valve opening); delayed and decreased P2 (absent if severe PS); right S4; ± cyanosis (if ASD or PFO)



Noonan syndrome: autosomal dominant; dysplastic pulmonary valve, pulmonary artery stenosis, ASD, HCM, developmental delay, facial dysmorphism, small stature, congenital lymphedema

LEOPARD syndrome: autosomal dominant; lentiginos, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genital organs, growth retardation, deafness, LVH

POSSIBLE COMPLICATIONS

- RVH
- Right heart failure \pm TR
- Pulmonary regurgitation (postoperative)
- Pulmonary artery dilatation (post-stenotic)
- Cyanosis in the presence of associated ASD or VSD
- Atrial arrhythmia (AF / flutter) or ventricular arrhythmia

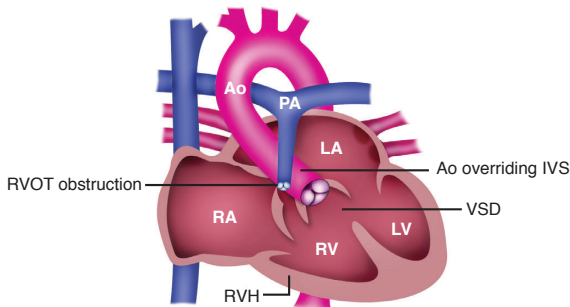
INDICATIONS FOR SURGERY

- a) Balloon valvuloplasty for **dome-shaped valvular stenosis with symptoms and maximum Doppler gradient > 50 mmHg** or mean gradient > 30 mmHg (I;C)
- b) Balloon valvuloplasty for **asymptomatic dome-shaped valvular stenosis and maximum Doppler gradient > 60 mmHg** or mean gradient > 40 mmHg (I;C)
- c) **Surgery if significant RVOT obstruction with:** dysplastic valve or supra-ventricular stenosis or subvalvular stenosis or associated pulmonary hypoplasia or severe associated PR (I;C)
- d) **Severe postoperative PR:** deterioration of functional class or deterioration of RV function or significant TR or flutter / AF or sustained ventricular arrhythmia (I;C)
- e) **Valvular stenosis with:** significant arrhythmia or ASD / VSD (with R \rightarrow L shunt) or recurrent endocarditis (IIa;C)
- f) **Double chamber RV** with significant mid-chamber obstruction (gradient > 50 mmHg on catheterization) (IIa;C)

PREGNANCY: well tolerated if RV pressure < 70% of LV pressure; valvuloplasty as required during pregnancy in the presence of severe refractory symptoms (ideally after first trimester)

7.10/ TETRALOGY OF FALLOT (TOF)

COMBINATION OF: **A)** Non-restrictive (subarterial) VSD; **B)** RVOT obstruction (infundibular, valvular or supra-ventricular); **C)** RVH; **D)** Aorta overriding the septum



CORRECTIVE SURGERY: **A)** Closure of the VSD; **B)** RVOT disobstruction; **C)** \pm infundibulectomy or subannular patch or transannular patch (induces significant PR) or RV - PA conduit (if congenital coronary artery anomalies crossing over the RVOT) or PVR or pulmonary valvotomy or pulmonary arterioplasty

ASSOCIATED ABNORMALITIES: right aortic arch; secundum ASD (pentalogy of Fallot); pulmonary trunk and peripheral pulmonary artery stenosis / hypoplasia; congenital coronary artery anomalies (LAD with ectopic origin crossing over the RVOT)

- > **DiGeorge syndrome** (15% of TOF): 22q11 deletion; facial dysmorphism, hypocalcemia, thymus hypoplasia, immune deficit, psychiatric illness, truncus arteriosus, interrupted aortic arch, double outlet RV

CLINICAL FEATURES (POST-CORRECTION): left parasternal heave; soft ejection murmur (RVOT); subtle and soft diastolic pulmonary murmur (PR); \pm absent P2; \pm holosystolic murmur in the case of residual VSD; \pm AR murmur

ECG: RBBB; wide QRS (**QRS > 180 ms is a risk factor for VT**)

+

INVESTIGATIONS: **A)** TTE; **B)** MRI (RV and LV function and dimensions; PR; TR; RVOT; pulmonary arteries; shunt; Ao); **C)** Stress test (exercise capacity); **D)** Holter; **E)** Electrophysiological study PRN

TTE: Severe PR if **the continuous Doppler regurgitation envelope is dense and reaches zero before the end of diastole** (equalization of pressures on either side of the valve) or if PHT < 100 msec

+

POST-CORRECTION COMPLICATIONS

- > **Pulmonary regurgitation**
- > **RV dysfunction / RV dilatation (\pm TR)**
- > Residual RVOT obstruction (subvalvular, valvular or supra-valvular) / peripheral pulmonary artery stenosis (causing RV pressure overload)
- > Residual VSD
- > Infundibular aneurysm
- > LV dysfunction
- > Aortic root dilatation / Progressive AR
- > Arrhythmia: atrial flutter; IART; AF; AV block
- > VT (RVOT heavily scarred from surgical intervention); sudden death (0.2% year)
- > Endocarditis

INDICATIONS FOR POST-CORRECTION SURGERY (IIA;C)

- Severe PR** with: symptoms or moderate-to-severe RV dilatation (**end-diastolic volume > 170 mL/m²; end-systolic volume > 85 mL/m²**) or moderate-to-severe RV dysfunction (**RVEF < 45 %**) or moderate-to-severe TR or atrial or ventricular arrhythmia
- Residual VSD** with shunt > 1.5:1
- Moderate to severe RVOT obstruction** (peak Doppler gradient > 50 mmHg)
- Severe AR** with symptoms or LV dysfunction
- Aortic root > 55 mm**
- RVOT aneurysm or false aneurysm**
- Combination** of residual VSD and/or residual PS and PR inducing RV dilatation / dysfunction or symptoms

+

SURGICAL OPTIONS: **A)** PVR (bioprosthesis or cadaver) \pm tricuspid annuloplasty; **B)** Percutaneous pulmonary valve inserted into a pre-existing RV-PA conduit; **C)** Infundibular resection or RVOT patch or transannular patch or valved conduit if obstruction persists

VENTRICULAR ARRHYTHMIA: Risk factors: **A)** Inducible VT on EPS; **B)** QRS > 180 ms; **C)** History of palliative shunt; **D)** Significant PR or RVOT obstruction; **E)** Advanced age at the time of complete correction; **F)** NSVT on Holter; **G)** RV or LV dysfunction; **H)** Syncope; **I)** Severe RV dilatation (> 150-180 ml/m²)

> **Secondary prevention:** ICD indicated

> **Primary prevention:** indication for ICD determined on an individual basis according to the risk of sudden death (risk of frequent inappropriate shocks)

PREGNANCY: risk of right heart failure in the presence of RVOT obstruction and/or severe PR and/or RV dysfunction; screen for 22q11 deletion

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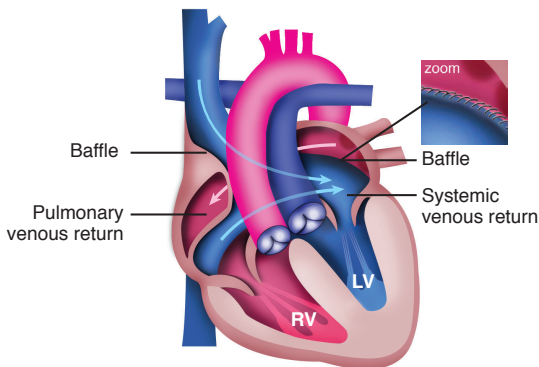
7.11/ TRANSPOSITION OF THE GREAT ARTERIES (D-TGV)

Atrioventricular concordance and ventriculoarterial discordance (the RA is connected to the morphological RV which is connected to the Ao; the LA is connected to the morphological LV which is connected to the PA); incompatible with life in the absence of operation (2 parallel circuits)

POSITION OF THE AORTA: anterior and to the right of the PA (connected to the RV)

ASSOCIATED ABNORMALITIES: VSD; LVOT obstruction; ASD; CoA; congenital coronary artery anomalies

ATRIAL SWITCH: MUSTARD (OR SENNING) PROCEDURE



The majority of adults have undergone this procedure (but this operation was replaced by arterial switch in about 1990); the blood is redirected to the atria by means of a conduit (baffle) made from pericardium or Dacron allowing physiological correction (systemic venous blood is redirected towards the subpulmonary LV; pulmonary venous blood is redirected towards the subaortic RV)

CLINICAL FEATURES: Single S2 (loud A2; P2 is inaudible as the PA is posterior); left parasternal heave; holosystolic murmur of the systemic AV valve

ECG: RVH; block - bradycardia; atrial arrhythmia

CXR: Egg-shaped heart (narrow mediastinum due to parallel great vessels); retrosternal aorta (lateral view)

TTE: Ao and PA are parallel; phasic flow in the baffle with **peak velocity < 1 m/s**; agitated-saline to evaluate baffle leak or stenosis

COMPLICATIONS

- a) **Systemic RV failure (+ TR)**
- b) Systemic RV ischemia (perfused only by the RCA)
- c) Systemic AV valve regurgitation (abnormal septal geometry)
- d) Obstruction of the baffle (SVC; IVC)
- e) Baffle leak (paradoxical embolism; cyanosis)
- f) Subpulmonary obstruction (abnormal LV geometry)
- g) Arrhythmias: atrial flutter; IART; SSS; AV block
- h) VT - Sudden death (risk factors: RV dysfunction; age; supraventricular arrhythmia; QRS > 140 ms)

INDICATIONS FOR POST-MUSTARD SURGERY (IIA;C)

- a) **Moderate-to-severe systemic AV valve regurgitation**
- b) **SVC or IVC obstruction** (dilatation + stent in baffle)
- c) **Pulmonary vein obstruction** (post-Senning procedure)
- d) **Baffle leak with:** significant shunt ($Q_p:Q_s > 1.5:1$) or symptoms or PHT or progressive ventricular dilatation / dysfunction or need for pacemaker transvenous lead or R→L shunt with cyanosis (percutaneous closure of the leak)
- e) **Symptomatic tachyarrhythmia:** ablation
- f) **Bradyarrhythmia:** pacemaker with endovenous lead in the absence of baffle stenosis or baffle leak
- g) **Consider transplant** if severe systemic RV dysfunction

PREGNANCY: avoid pregnancy in the presence of moderate-to-severe systemic RV dysfunction and/or severe systemic AV valve regurgitation

ARTERIAL SWITCH: JATENE PROCEDURE

Switching of the Ao and PA; the PA is replaced anteriorly (Lecompte maneuver); the coronary arteries are reimplemented; the LV becomes subaortic

COMPLICATIONS

- a) Obstruction of the aorta and pulmonary artery at the sites of surgical anastomosis
- b) Subpulmonary or PA or pulmonary arterial branch obstruction following Lecompte maneuver
- c) Aortic root dilatation / AR
- d) Stenosis of the coronary ostia (regular screening for CAD is indicated)

INDICATIONS FOR POST-JATENE SURGERY (IIA;C)

- a) **Significant PA obstruction** (subvalvular, supra-ventricular or arterial branch)
- b) **Coronary artery obstruction**
- c) **Severe AR**
- d) **Severe Ao dilatation > 55 mm**

RASTELLI PROCEDURE

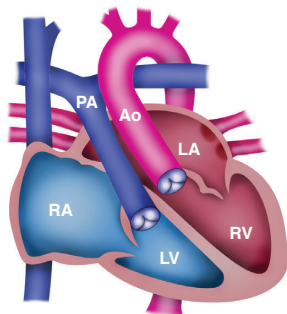
For treatment of D-TGV with VSD and RVOT obstruction

PROCEDURE: **A)** LVOT tunneled to the Ao by an intracardiac patch through the VSD; **B)** RV - PA extracardiac valved conduit

7.12/ CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES (L-TGV)

DOUBLE DISCORDANCE (atrioventricular and ventriculoarterial): the circulation is corrected physiologically; the morphological RV is systemic (subaortic)

POSITION OF THE AORTA: anterior and to the left of the PA



ASSOCIATED ABNORMALITIES: abnormalities of the systemic T valve (Ebstein-like malformation); VSD; PS; dextrocardia

ECG: AV block (fragile His bundle which is displaced anteriorly and laterally); septal activation from R to L (septal Q waves absent on left precordial leads, but present on right precordial and inferior leads); accessory pathway

CLINICAL FEATURES: Palpable A2 (anterior Ao); inaudible P2 (posterior PA); holosystolic murmur due to systemic AV valve regurgitation

COMPLICATIONS

- Progressive systemic AV valve regurgitation (T valve)
- Progressive systemic RV dysfunction
- Systemic RV ischemia (only perfused by the RCA)
- Complete AV block (2% / year)
- Atrial arrhythmia: AF; IART; accessory pathway
- VT - sudden death

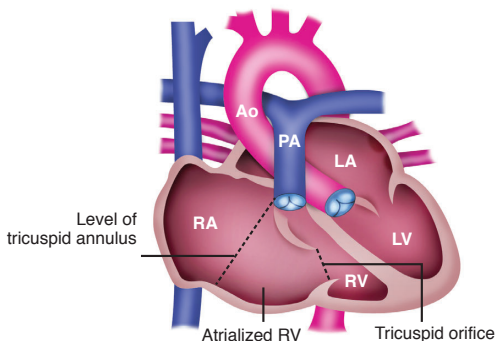
INDICATIONS FOR SURGERY

- Moderate-to-severe systemic AV valve regurgitation (IIa;B)
- Deterioration of the systemic RV (IIa;C): consider heart transplantation

PREGNANCY: avoid pregnancy if RVEF < 40% and/or moderate-to-severe TR

7.13/ EBSTEIN ANOMALY

Apical displacement of the tricuspid valve $> 8 \text{ mm/m}^2$ (septal and posterior leaflets) with elongated / redundant anterior leaflet; atrialized RV (small volume functional RV)



ASSOCIATED ABNORMALITIES: **A)** Accessory pathway(s) (25% of patients; 50% have multiple pathways); **B)** secundum ASD or PFO \pm cyanosis (50% of patients); **C)** RVOT obstruction (by T valve); VSD; mitral valve disease

CLINICAL FEATURES: \pm V wave in jugular veins (often absent due to severe RA dilatation); left parasternal heave; split S1 with \nearrow T1; split S2 (RBBB); right S3; lower left parasternal holosystolic murmur (\nearrow on inspiration); systolic clicks; \pm cyanosis; low output state; signs of right heart failure

ECG: RA dilatation (**Himalayan P waves**); low voltage; \pm pre-excitation; RBBB; Q waves in V1 (as far as V4) and inferior leads; AF - flutter

CXR: "water bottle heart": RA dilatation and left convexity (dilatation of the RV infundibulum); \searrow vascularization

COMPLICATIONS

- Severe TR**
- Right heart failure / Dilatation of right chambers**
- Arrhythmias: flutter; AF; AT; accessory pathway(s)
- Sudden death (pre-excited atrial arrhythmia or VT)
- Cyanosis - paradoxical embolism in the presence of PFO or ASD
- RVOT obstruction due to the abnormal tricuspid valve
- Tricuspid stenosis or prosthetic valve dysfunction post-surgery

INDICATIONS FOR SURGERY (I;B)

- Severe TR** with NYHA III - IV or deterioration of functional class
- Progressive RV dysfunction or dilatation**
- Progressive cardiomegaly** on CXR (cardiothoracic ratio $> 65\%$)
- Cyanosis** with resting $\text{SaO}_2 < 90\%$ (closure of ASD)
- Paradoxical embolism** (closure of ASD)
- Arrhythmia / WPW:** ablation by catheter or surgical cryoablation

REPAIR: feasibility according to: **A) Length and mobility of the anterior leaflet (creation of a monoleaflet valve); B) Size of the residual RV > 1/3 of total RV**

OTHER SURGICAL OPTIONS

- > **Conventional TVR**
- > **Bidirectional cavopulmonary connection (bidirectional Glenn):** decreases preload and workload of the small RV
- > **Fontan procedure** in the presence of a hypoplastic RV
- > **Heart transplantation**

PREGNANCY: well tolerated in the absence of cyanosis / right heart failure / arrhythmia

7.14/ MARFAN SYNDROME

Autosomal dominant; FBN1 gene mutation (> 1,000 mutations have been reported)

COMPLICATIONS: Aortic root dilatation; aortic dissection; AR; MVP - MR; left heart failure; tricuspid valve prolapse - TR

MANAGEMENT

- a) BB (↘ dP/dT) and ARB
- b) Target SBP < 120 mmHg (BB; ARB)
- c) Avoid isometric exercise - competitive / contact sports
- d) MRI indicated to evaluate all of the aorta; regular follow-up is recommended

TTE FOLLOW-UP	MRI OR CT ANGIOGRAPHY
Annually	Every 3 to 5 years (more frequent if dilatation / imminent indication for surgery / 1 year postop / recent dissection)

INDICATIONS FOR SURGERY (I;B)

- a) **Ascending aorta > 50 mm**
- b) **Ao > 45 mm:** with: progression > 5 mm/year or progressive AR with probable valve preservation or family history of aortic dissection with Ao < 50 mm or severe MR requiring surgery
- c) **Ao > 40 mm before pregnancy**
- d) **Other regions of the Ao** between 50-60 mm or progressive dilatation

SURGICAL OPTIONS: **A) Bentall procedure:** replacement of ascending Ao with valved graft; **B) David procedure:** replacement of the ascending Ao with graft and resuspension of the native aortic valve (valve sparing)

PREGNANCY: risk of transmission (autosomal dominant); MRI imaging of the entire Ao; TTE every 4-8 weeks; BB; avoid ↗ dP/dT during delivery; cesarean section if unstable aorta (> 40-45 mm)

- > **Pregnancy contraindicated if Ao > 45 mm** (risk of aortic dissection)
- > **If Ao ≥ 40 mm:** referral for surgery is recommended if contemplating pregnancy



GHENT CRITERIA

SYSTEM	MAJOR CLINICAL SIGNS	MINOR CLINICAL SIGNS	DEFINITION OF SYSTEM INVOLVEMENT
Skeletal	<ul style="list-style-type: none"> • <i>Pectus carinatum</i> • Surgical <i>Pectus excavatum</i> • Long limbs <ul style="list-style-type: none"> ➢ Arm span to height ratio > 1.05 or ➢ Upper segment to lower segment ratio • Long fingers <ul style="list-style-type: none"> ➢ Wrist sign and thumb sign • Scoliosis > 20° or spondylolisthesis • Maximum elbow extension < 170° • Flat foot • Acetabular protrusion (hip x-ray) 	<ul style="list-style-type: none"> • Moderate <i>Pectus excavatum</i> • Joint hypermobility • Arched palate with overlapping teeth • Characteristic facies 	<p>Major ≥ 4 major signs</p> <p>Minor ≥ 2 major signs or 1 major and 2 minor signs</p>
Ocular	<ul style="list-style-type: none"> • Lens dislocation 	<ul style="list-style-type: none"> • Flat cornea • Elongated eyeball • Myopia 	<p>Major 1 major sign</p> <p>Minor ≥ 2 minor signs</p>
Cardio-vascular	<ul style="list-style-type: none"> • Aortic root dilatation • Aortic dissection 	<ul style="list-style-type: none"> • MVP • Pulmonary trunk dilatation < 40 years • MAC < 40 years • Dilatation or dissection of the descending thoracic aorta or abdominal aorta < 50 years 	<p>Major ≥ 1 major sign</p> <p>Minor ≥ 1 minor sign</p>
Pulmonary		<ul style="list-style-type: none"> • Spontaneous pneumothorax • Apical bulla (CXR or CT) 	<p>Minor ≥ 1 minor sign</p>
Cutaneous		<ul style="list-style-type: none"> • <i>Striae atrophicae</i> (unexplained) • Recurrent incisional herniae 	<p>Minor ≥ 1 minor sign</p>
Dura mater	<ul style="list-style-type: none"> • Lumbosacral dural ectasia (CT or MRI) 		<p>Major 1 major sign</p>
Genetic	<ul style="list-style-type: none"> • 1 first-degree relative with diagnostic criteria • FBN1 gene mutation causing Marfan 		

Diagnosis established:

- 1 system with major involvement + 1 system with minor involvement + 1 genetic criterion
- 2 systems with major involvement + 1 system with minor involvement

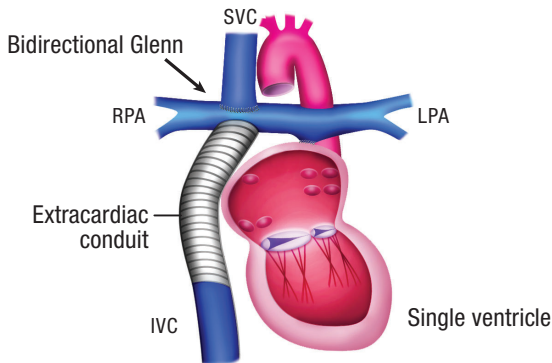
Lœys BL, Dietz HC, Braverman AC, et al. *J Med Genet* 2010; 47:476-485

7.15/ FONTAN PROCEDURE

Palliative procedure in the presence of a single ventricle (anatomical or functional); systemic venous return redirected to PA, short-circuiting the subpulmonary ventricle

PREREQUISITES: Mean PAP < 15 mmHg with normal-sized PA, normal function of the single ventricle, absence of any significant AV valve regurgitation

STEPS OF THE MODIFIED FONTAN PROCEDURE: 1) **Bidirectional cavopulmonary connection (bidirectional Glenn):** connection between the SVC and R or L pulmonary arteries; 2) **Connection of IVC to PA** (lateral conduit or extracardiac conduit or intracardiac conduit) with pulmonary trunk ligation



FACTORS OF HEMODYNAMIC DETERIORATION

- Any \nearrow filling pressure of the systemic ventricle
- Obstruction to systemic venous return (thrombosis or obstruction of Fontan; \nearrow PVR; pulmonary arteries stenosis; pulmonary vein compression)
- Arrhythmia (risk of hemodynamic deterioration and thrombus)

CLINICAL FEATURES: JVD but nonpulsatile; single S1 and S2; absence of murmur (except in the case of AV valve regurgitation or subaortic obstruction); hepatomegaly / leg edema / ascites

COMPLICATIONS

- Intra-Fontan thrombus:** predisposed by stasis and atrial arrhythmia; leads to Fontan obstruction / pulmonary embolism / paradoxical embolism
- Fontan obstruction** (at anastomotic sites or by thrombus)
- Right pulmonary vein compression** by the interatrial septum or the dilated RA
- Arrhythmia:** IART; flutter; AF; SSS; AV block
- Cyanosis in the presence of a R \rightarrow L shunt:** systemic venous collateral to pulmonary veins; pulmonary AVM; residual ASD; fenestrated Fontan; hepatopulmonary syndrome
- Ventricular dysfunction / systemic AV valve regurgitation**
- Protein-losing enteropathy:** anasarca; diarrhea; \nearrow fecal alpha-1-antitrypsin and hypoalbuminemia
- Congestive hepatopathy** (or even cardiac cirrhosis)

MANAGEMENT

- A/C** if thrombus or stasis or thromboembolism or ASD or fenestration or atrial arrhythmia
- Single-ventricle failure:** consider ACE inhibitors - BB; sildenafil; transplant; mechanical support
- Aggressive treatment of atrial arrhythmias:** look for a hemodynamic cause; TEE prior to ECV; AAD; A/C; catheter ablation; conversion to extracardiac Fontan with intraoperative Maze
- When a pacemaker is indicated:** epicardial ventricular lead
- Protein-losing enteropathy:** diuretics - aldactone; eliminate obstruction or arrhythmia; dietary support; IV albumin; corticosteroids; sildenafil; Fontan fenestration; transplant

INDICATIONS FOR REOPERATION (I;C)

- Obstruction** to systemic venous return (revision of the Fontan or angioplasty / stenting or conversion of Fontan or thrombectomy)
- Obstruction** to pulmonary venous return (conversion to extracardiac Fontan)
- Moderate-to-severe systemic AV valve **regurgitation**
- Symptomatic cyanosis** with venovenous collaterals or pulmonary AVM (catheter occlusion)
- Residual ASD or fenestrated Fontan with significant R→L shunt (percutaneous closure)
- Subaortic stenosis** with peak-to-peak gradient > 30 mmHg
- Protein-losing enteropathy** with Fontan obstruction (revision of the Fontan or angioplasty / stenting) or with elevation of systemic venous pressures (consider fenestration)
- Symptomatic and refractory atrial arrhythmia** (conversion to extracardiac Fontan with intraoperative Maze)

PREGNANCY: increased risk of all Fontan-specific complications; risk of spontaneous abortion / IUGR / prematurity; follow-up by an experienced, multidisciplinary team

7.16/ EISENMENGER SYNDROME

Obstructive pulmonary vascular disease secondary to communication between pulmonary and systemic circulations (L→R shunt), leading in the long term to irreversible elevation of PAP and PVR (to systemic levels) and reversal of the shunt (R→L)

CLINICAL FEATURES: Central cyanosis (differential cyanosis in the presence of patent ductus arteriosus); clubbing; JVD (prominent A wave; prominent V wave in the presence of TR); signs of PHT

ECG: RAH; RVH; right axis deviation; atrial arrhythmia

CXR: dilatation of central pulmonary arteries ± calcification; dilatation of right chambers

COMPLICATIONS

- RV dysfunction**
- Complications of cyanotic heart disease:** erythrocytosis; bleeding; CRF; hyperuricemia / gout; cholelithiasis
- Intrapulmonary hemorrhage / hemoptysis
- Pulmonary artery aneurysm
- Pulmonary artery thrombosis / Pulmonary embolism
- Stroke - TIA; paradoxical embolism
- Brain abscess
- Arrhythmias: AF; flutter; VT
- Sudden death
- Endocarditis

MANAGEMENT

- Correct iron deficiency, when present
- Aggressive treatment of arrhythmia
- Noncardiac surgery: multidisciplinary preoperative assessment in a tertiary institution
- Pregnancy contraindicated
- Avoid dehydration - hemorrhage - anemia
- Avoid NSAID - vasoactive agents (which \nearrow the shunt and cyanosis) - estrogens - nephrotoxins
- Air filter on IV lines
- Avoid vigorous physical exercise
- Dental hygiene and prophylactic antibiotics
- Investigate hemoptysis (CXR; CBC; CT scan; embolization PRN)
- Influenza - pneumococcus vaccination

TREATMENT OF PHT

- First-line endothelin antagonists (Bosentan; Macitentan)
- PDE-5 inhibitors or prostanoids

LUNG \pm HEART TRANSPLANT: in the case of refractory symptoms with estimated 1-year survival < 50%; contraindicated in the presence of multiple pleuropulmonary collaterals

7.17/ CYANOTIC HEART DISEASE

R \rightarrow L shunt (deoxygenated blood enters the systemic circulation); chronic hypoxemia

SECONDARY ERYTHROCYTOSIS (\nearrow EPO)

- \triangleright **Hyperviscosity (Hct > 65% and Hb > 20 g/dL):** headache; faintness; tiredness; disorders of concentration; visual disorders; paresthesia; tinnitus; myalgia; intraoperative bleeding
 - **Treatment:** phlebotomies (if patient is iron-repleted and well hydrated)
 - **Treat any iron deficiency** (as microcytosis can cause hyperviscosity and is a risk factor for stroke); beware of rebound effect
- \triangleright **Bleeding / clotting abnormalities** (if severe bleeding: FFP; vitamin K; cryoprecipitates; DDAVP; platelets)

OTHER COMPLICATIONS: Stroke - TIA; cerebral hemorrhage; paradoxical embolism; brain abscess; CRF; proteinuria; hyperuricemia; gout; hypertrophic osteoarthropathy (arthralgia); scoliosis; cholelithiasis

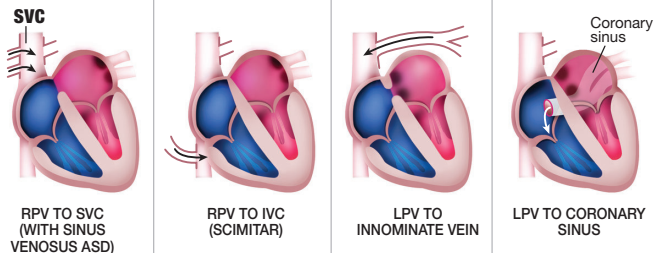
- \triangleright Beware of nephrotoxic agents, including contrast agents

BASIC WORK-UP: SaO₂; CBC; ferritin; transferrin; iron saturation; \pm folate; \pm vitamin B12; PT-PTT; renal function; uric acid

PALLIATIVE SHUNTS (systemic to pulmonary): objective: improve pulmonary blood flow and cyanosis

- \triangleright **Blalock-Taussig:** subclavian artery to pulmonary artery (modern: graft connecting the two arteries, preserving perfusion of the upper limb)
- \triangleright **Waterston:** Ascending Ao to right PA
- \triangleright **Potts:** Descending Ao to left PA
- \triangleright **Physical examination:** Continuous murmur (except in the presence of stenosis / occlusion / significant PHT)
- \triangleright **Complications:** PHT; distortion of PAs; stenosis / aneurysm at the site of anastomosis; heart failure (volume overload); arrhythmias

7.18/ ANOMALOUS PULMONARY VENOUS RETURN



CONSEQUENCES AND CLINICAL FEATURES: similar to ASD

INDICATION FOR SURGERY: dilatation of right chambers

SCIMITAR SYNDROME: pulmonary veins (right lung) drain into the IVC; scimitar appearance on CXR; \pm hypoplasia of right lung

7.19/ CONGENITAL CORONARY ARTERY ANOMALIES

ECTOPIC ORIGIN OF A CORONARY ARTERY

1 % of the population

CLINICAL FEATURES: sudden death; retrosternal chest pain; arrhythmia; LV dysfunction; syncope

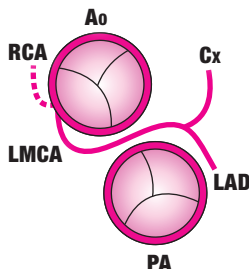
DETECTION: coronary CT angiography (or cardiac MRI); cholelithiasis

➤ Look for ventricular arrhythmia during exercise testing

INDICATIONS FOR SURGERY

(reimplantation; marsupialization)

- Coronary artery coursing between the great vessels with **documented ischemia** (I;B)
- Ectopic origin of **LMCA** (opposite sinus) coursing between the Ao and the PA (I;B)
- Ectopic origin of the **right coronary artery** (opposite sinus) coursing between the Ao and the PA with documented ischemia (I;B)
- Ectopic origin of the **LAD** coursing between the Ao and the PA (IIb;C)



ALCAPA SYNDROME

Anomalous left coronary artery arising from the pulmonary artery

CLINICAL FEATURES: ischemia; LV dysfunction; MI; ventricular arrhythmia; sudden death; may be well tolerated in the presence of collaterals of the RCA

INDICATIONS FOR SURGERY (coronary reimplantation)

- > All patients with **ALCAPA syndrome** (I;C)

CORONARY ARTERIOVENOUS FISTULA

Communication between a coronary artery and a heart chamber (RA; RV) or a vein (coronary sinus; vena cava; pulmonary vein) or sometimes the PA

CLINICAL FEATURES: continuous left parasternal murmur

COMPLICATIONS

- Dilatation of the nutrient coronary artery
- Rupture - dissection
- Myocardial ischemia distal to the fistula
- Endarteritis
- Left heart failure

INDICATIONS FOR SURGERY (percutaneous closure by embolization or surgical closure)

- Large fistula - Qp:Qs > 1.5 : 1 (I;C)
- Small to moderate fistula with: ischemia or arrhythmia or LV dysfunction or LV dilatation or endarteritis (I;C)

CONGENITAL SINUS OF VALSALVA ANEURYSM

RUPTURE: Sudden chest pain and dyspnea; continuous AV shunt with possible left and right heart failure; bounding pulse; continuous murmur ± thrill

- Ruptured aneurysm of the right sinus of Valsalva: Ao - RVOT fistula
- Ruptured aneurysm of the non-coronary sinus: Ao - RA fistula
- Ruptured aneurysm of the left sinus of Valsalva: Ao - LA fistula

DDX: Infectious (endocarditis); Inflammatory - Vasculitis; Marfan; latrogenic

MYOCARDIAL BRIDGE ("MILKING")

Intramyocardial coronary segment (usually LAD)

Compression of the coronary segment with each systole

CONSEQUENCES: usually none; sometimes ischemia - angina - LV dysfunction - arrhythmia / VT - sudden death

MANAGEMENT: BB; CCB; PCI or CABG if severe refractory ischemia

7.20/ VASCULAR RING

Malformation of the aortic arch associated with **compression of the esophagus and/or trachea** (dysphagia, respiratory symptoms, stridor)

- Double aortic arch
- Right aortic arch; associated with Kommerell's diverticulum compressing the trachea (diverticulum at the junction of the left subclavian artery and the descending aorta)
- Aberrant origin of the right subclavian artery (posterior to the esophagus)
- Retroesophageal descending aorta (compression of the trachea)

7.21/ COR TRIATRIATUM

Fibromuscular diaphragm dividing the LA into two chambers

Severity varies according to the degree of stenosis; nonobstructive form (benign) versus obstructive form (leads to PHT)

Management similar to that of MS

7.22/ HEART DISEASE IN PREGNANT WOMEN

HEMODYNAMIC CHANGES DURING PREGNANCY

HEMODYNAMIC CHANGES	CONSEQUENCES
↗ 40-50% of plasma volume	Risk of congestion
↗ 10-20% of HR	Poorly tolerated MS
↗ 30-50% of cardiac output	
↘ Peripheral resistance (especially ↘ DBP)	Tolerated poorly stenotic lesions (increased gradient)
↗ Venous pressure in legs	Risk of stasis / DVT
Hypercoagulability	Increased thromboembolic risk

NORMAL PHYSICAL EXAMINATION OF THE PREGNANT WOMAN

↗ HR; normal or slightly ↗ CVP; Hyperdynamic state (pulse; apex); Apex may be broadened and slightly lateralized; leg edema is frequent

Accentuated S1 - accentuated splitting; S2 may appear to be constantly split at the end of pregnancy; S3 is frequent; left parasternal ejection murmur $\leq 3/6$; continuous murmur (cervical venous "hum" or breast murmur)

MATERNAL RISK OF CARDIAC EVENTS

STRESS TEST: high-risk pregnancy if $< 70\%$ of predicted functional capacity

CARPREG SCORE (1 point each):

<ol style="list-style-type: none"> History of heart failure - TIA - Stroke - Arrhythmia NYHA \geq III or cyanosis Mitral valve area $< 2 \text{ cm}^2$ or Aortic valve area $< 1.5 \text{ cm}^2$ or LVOT gradient $> 30 \text{ mmHg}$ Systemic ventricle systolic function $< 40\%$ 	<p>Risk of cardiac event during pregnancy:</p> <ul style="list-style-type: none"> 0 point: 5 % 1 point: 27 % ≥ 2 points: 75 %
--	--

* Does not take PHT - mechanical valve - aortopathy into account

Siu SC, Sermer M, Colman JM, et al. Circulation 2001; 104:515-521.

WHO CLASSIFICATION

STAGE I: LOW-RISK PREGNANCY

- Uncomplicated, small or mild PS or patent ductus arteriosus or MVP
- Successfully repaired simple lesions (ASD; VSD; patent ductus arteriosus; anomalous pulmonary venous drainage)
- Isolated APC and PVC

STAGE II: MILD-TO-MODERATE RISK PREGNANCY

- Unrepaired ASD or VSD
- Repaired TOF
- Most arrhythmias

Stage II or III, depending on severity

- Mild LV dysfunction
- HCM
- Valvular heart disease not considered to be WHO stage I or IV
- Marfan syndrome without Ao dilatation
- Bicuspid aortic valve with Ao < 45 mm
- Repaired CoA

STAGE III: HIGH-RISK PREGNANCY (EXPERT FOLLOW-UP RECOMMENDED)

- Mechanical valve
- Systemic RV
- Fontan
- Cyanotic heart disease
- Complex congenital heart disease
- Marfan: Ao 40-45 mm
- Bicuspid aortic valve: Ao 45-50 mm

STAGE IV: PREGNANCY CONTRAINDICATED

- Severe pulmonary arterial hypertension
- Severe LV dysfunction (LVEF < 30% - NYHA III or IV)
- Previous peripartum cardiomyopathy with residual impairment of LV function
- Severe MS or severe AS
- Marfan: Ao > 45 mm
- Bicuspid aortic valve: Ao > 50 mm
- Unrepaired CoA

BICUSPID AORTIC VALVE STENOSIS

Pregnancy contraindicated if ascending Ao > 50 mm (or > 25 mm/m²)

- > In the presence of Ao dilatation: TTE every 4-8 weeks; BB

SEVERE AORTIC STENOSIS: avoid pregnancy (particularly if symptoms or LV dysfunction or abnormal stress test); risk of hemodynamic instability during delivery; percutaneous valvuloplasty PRN in the presence of severe symptoms

MITRAL STENOSIS

Moderate-to-severe MS is poorly tolerated; deterioration due to tachycardia and ↗ cardiac output; risk of pulmonary congestion and PHT

BB (Metoprolol); valvuloplasty PRN if refractory NYHA III-IV

MITRAL REGURGITATION AND AORTIC REGURGITATION

Generally well tolerated if moderate regurgitation / NYHA \leq II / normal LV function and dimensions

Diuretics and vasoactive agents PRN; Surgery if refractory NYHA III-IV

PROSTHETIC VALVE

Follow-up by an experienced multidisciplinary team

MECHANICAL VALVE: significant maternal and fetal risks

- Thromboembolic risk (hypercoagulability of pregnancy)
- Risk associated with anticoagulation (fetal loss; placental hemorrhage; insufficient anticoagulation; embryopathy; management during delivery)

UNFRACTIONATED HEPARIN (IV OR SC): less effective than warfarin; adjusted according to aPTT 6h post-injection ($> 2 \times$ normal)

LMWH: bid; dose according to **anti-Xa level 4 h post-injection (target: 0.8-1.2 IU/mL)**; review once a week; replace by unfractionated heparin > 36 h before delivery

WARFARIN: risk of embryopathy during the first trimester (4-10%); **lower risk with Warfarin ≤ 5 mg daily**

WARFARIN DOSE ≤ 5 MG QD: continue Warfarin; replace by unfractionated heparin at the end of pregnancy prior to planned delivery

WARFARIN DOSE > 5 MG QD: LMWH or IV Heparin during first trimester; replace by Warfarin for 2nd and 3rd trimesters; then replace by unfractionated heparin prior to planned delivery

CYANOTIC HEART DISEASE

Pregnancy contraindicated if $\text{SaO}_2 < 85\%$

R \rightarrow L shunt increased by \searrow peripheral resistance

Maternal hypoxia alters fetal growth and survival

PULMONARY HYPERTENSION

Pregnancy contraindicated in the presence of severe pulmonary hypertension

EISENMENGER: maternal mortality as high as 50%



DILATED CARDIOMYOPATHY

Avoid pregnancy if LVEF $< 40\%$

PERIPARTUM CARDIOMYOPATHY

DEFINITION: "Idiopathic" cardiomyopathy with LV systolic dysfunction occurring around the last month of pregnancy or during the first 5 months post-partum

- Diagnosis of exclusion

RISK FACTORS: twin pregnancy, African American mother, advanced age, pre-eclampsia, smoking

MANAGEMENT: **A)** Hydralazine / Nitrates; **B)** BB (avoid Atenolol and Carvedilol; prefer beta-1 selective BB; Metoprolol is the best studied BB during lactation); **C)** Digoxin; **D)** Diuretics; **E)** Anticoagulate if intracardiac thrombus or LVEF < 35% or concomitant Bromocriptine

- ACE inhibitors (Captopril; Enalapril) are safe while breastfeeding
- Possible benefit of post-partum Bromocriptine (2-5 mg/day)
- Continue therapy with standard HF medications for ≥ 12 months

Normalization of LVEF in 50% of women (2 to 6 months)

Avoid subsequent pregnancy (**30% recurrence rate**)

HYPERTROPHIC CARDIOMYOPATHY

Autosomal dominant; variable penetrance

High-risk pregnancy if symptoms at baseline or significant baseline LVOT gradient

HYPERTENSION

PRE-EXISTING HTN: before pregnancy or < 20 weeks; rule out CoA

GESTATIONAL HYPERTENSION: *de novo* HTN (> 20 weeks after start of pregnancy); BP > 140/90 on 2 occasions; absence of proteinuria; returns to normal during the first 12 weeks postpartum

➢ **Management:** Labetalol; Methyldopa; Nifedipine

PRE-ECLAMPSIA: gestational HTN with the presence of proteinuria (> 300 mg/24 h or > 30 mg/mmol on urine spot test)

- **Risk factors:** primiparous; twin pregnancy; ≥ 40 years; BMI ≥ 35 kg/m²; family history of preeclampsia
- **Clinical features:** headache, blurred vision, abdominal pain, thrombocytopenia, abnormal LFTs, hemolysis, hyperreflexia - clonus, seizures, acute pulmonary edema, stroke
- **Management:** rest; sodium restriction; magnesium sulphate; delivery; IV Labetalol; Methyldopa; Nifedipine; IV Nitroglycerin; target SBP 140 to 160 mmHg and DBP 90 to 105 mmHg

ATRIAL FIBRILLATION

Anticoagulant according to embolic risk

CONTROL HR: Digoxin; BB (Metoprolol); CCB (Verapamil)

CONTROL RHYTHM: ECV; CCV (Procainamide); Flecainide / Sotalol

Continuous fetal monitoring during intervention / AAD

SUPRAVENTRICULAR TACHYCARDIA

ACUTE: Vagal maneuver or Adenosine or ECV; Metoprolol PRN; IV Procainamide; Continuous fetal monitoring during intervention

PROPHYLAXIS: Metoprolol or Digoxin; Flecainide / Sotalol PRN; Verapamil or ablation as 3rd line

CONTRACEPTION

Avoid estrogens in women with cyanotic heart disease, AF or flutter, mechanical prosthetic valve, Fontan, thromboembolic history or LVEF < 40%

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Peripheral Vascular Disease

08

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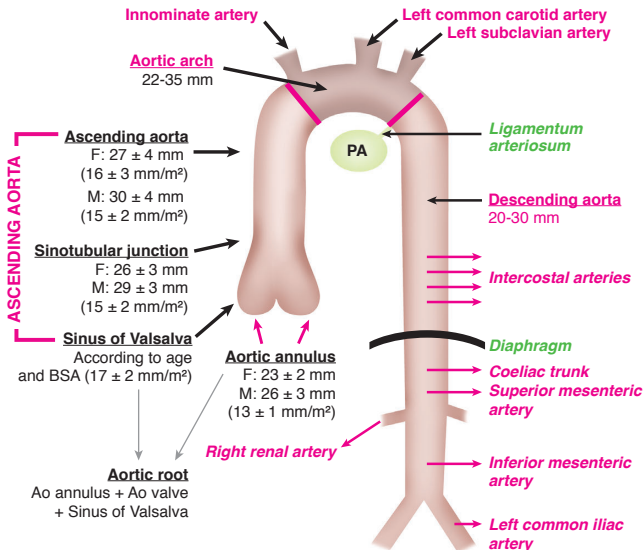
8.1/ ANEURYSM OF THE THORACIC AORTA

ANEURYSM: permanent and localized dilatation of an artery; **diameter > 150 %** of normal diameter (for age / gender / BSA) +

> **Ectasia:** arterial dilatation < 150% of normal diameter

> **Pseudo-aneurysm (false aneurysm):** **rupture** of arterial wall contained by hematoma and adjacent tissues +

NORMAL DIMENSIONS



RISK FACTORS

- > **Atherosclerotic / Degenerative** (media degeneration): HTN; smoking; COPD; family history
- > **Congenital**: Bicuspid aortic valve; Tetralogy of Fallot; CoA; VSD; Transposition of great arteries
- > **Genetic**: Marfan; Ehlers-Danlos type IV; Turner; Loeys-Dietz; Noonan; Familial thoracic aortic aneurysm syndrome
- > **Inflammatory**: Takayasu; Giant cell arteritis; Behçet; Ankylosing spondylitis; Spondyloarthropathies; SLE; Sarcoidosis
- > **Infectious**: Syphilis; Salmonella; Staphylococcus; HIV

PRESENTATION: Asymptomatic; Aortic dissection; Aortic rupture; AR; Infectious aortitis; Compressive symptoms (recurrent laryngeal nerve; trachea; esophagus; SVC syndrome); Pain (neck; jaw; back; interscapular); Embolism (thrombus or cholesterol crystals); Fistula (aorto-esophageal; aortobronchial)

ECHOCARDIOGRAPHY: diameter at end-diastole using the leading-edge of the anterior wall to the leading of the posterior wall +

CT SCAN AND MRI: measurement of outer diameter +

CXR: large mediastinum; prominent aortic knob; trachea deviated to the right

MANAGEMENT

RISK FACTOR CONTROL: HTN; Lipids; Smoking

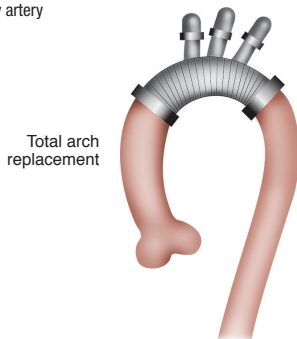
BB AND ACE INHIBITORS / ARB

AVOID ISOMETRIC EXERCISES

INDICATIONS FOR SURGERY – ASCENDING AORTIC ANEURYSM	
Degenerative ascending aortic aneurysm	≥ 55 mm
Progressing aneurysm	> 5 mm / year
Symptomatic aneurysm	Compressive symptoms; Pain
Ao valve or CABG surgery	> 45 mm
Bicuspid aortic valve	> 55 mm (or > 50 mm with family history of dissection or progression ≥ 5 mm / year)
Marfan	40-50 mm (▶▶ Genetic aortic syndromes)
Marfan or Genetic Syndrome or Bicuspid aortic valve	Maximum Ao area (cm ²) / Patient's height (m) > 10
Løys-Dietz	≥ 42 mm (TEE) or ≥ 44 mm (CT or MRI)
Turner	> 25 mm/m ²
SURVEILLANCE – ASCENDING AORTIC ANEURYSM	
Aneurysm 35 - 44 mm	<ul style="list-style-type: none"> • Ensure stability with follow-up assessment 6 months after diagnosis • Stable → Imaging every 1-3 years (progression $\approx 1 - 2$ mm / year)
Aneurysm 45 - 54 mm	Imaging after 3-6 months (stability) then every 6-12 months
Pregnancy	Imaging every 6-8 weeks (until 3 months postpartum)

ANEURYSM OF AORTIC ARCH

SURGERY: requires profound hypothermia and circulatory arrest; temporary cerebral perfusion via the right axillary artery



SURGICAL OPTIONS: Resection of the proximal hemi-arch; Total arch replacement; Stent with reimplantation of innominate arteries...

- **Elephant trunk procedure:** aneurysm of the aortic arch and descending aorta; allows subsequent stenting of the descending aorta

MANAGEMENT – ANEURYSM OF THE AORTIC ARCH	
Isolated aneurysm of the aortic arch > 55 mm or compressive symptoms	Surgery (if acceptable surgical risk)
Aneurysm of the aortic arch < 40 mm	Imaging every 1-2 years
Aneurysm of the aortic arch > 40 mm	Imaging every 6-12 months

ANEURYSM OF THE DESCENDING THORACIC AORTA

MANAGEMENT – ANEURYSM OF THE DESCENDING THORACIC AORTA	
Degenerative or traumatic aneurysm > 55 mm	TEVAR (when technically feasible)
Chronic dissection + [refractory symptoms or aneurysm > 55 mm or progression of diameter > 4 mm/year]	TEVAR (open surgery when TEVAR is contraindicated)

SURGICAL PROCEDURE: CPB with retrograde femoral perfusion

- **Risk of spinal cord ischemia**

THORACIC ENDOVASCULAR AORTIC REPAIR (TEVAR): stent deployment requires a normal aortic segment > 20 mm above and below the aneurysm (with diameter < 40 mm) and adequate vascular access

- **Contraindications:** Severe Ao atherosclerosis (risk of atheroembolism); severe PAD (limiting femoral access)
- **Regular long-term surveillance following TEVAR:** CTscan or MRI after 1, 6 and 12 months and then yearly (or every 2 years if stable course)
- **Complications:** Stroke; Atheroembolism; Spinal cord ischemia; Paraplegia; MI; Ventricular arrhythmia; ARF; Transformation from type B to type A dissection; Stent fracture; Stent migration; Infection; Occlusion of arterial branches (subclavian; mesenteric; celiac trunk; renal)
 - **Endoleak:** persistence of blood flow outside of the stent lumen towards the aneurysm sac

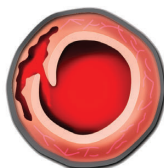
TYPE I ENDOLEAK	Reperfusion and filling of the aneurysm sac via a leak in the proximal or distal portion of the stent (requires treatment)
TYPE II ENDOLEAK	Retrograde flow in the aneurysm sac via a branch artery (intercostal; lumbar; mesenteric) (observation)
TYPE III ENDOLEAK	Separation of stent components (fracture; separation) (requires treatment)

8.2/ ACUTE AORTIC SYNDROME

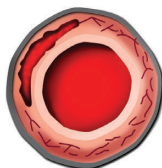
AORTIC DISSECTION

Tear of the media with bleeding inside the media and along the arterial wall

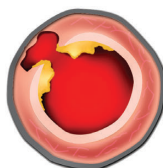
Acute aortic syndrome



Ao dissection



Intramural hematoma



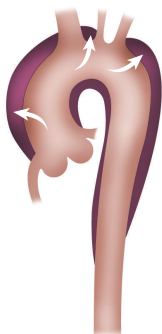
Penetrating atherosclerotic ulcer

STANFORD CLASSIFICATION

Type A	Involves the ascending Ao
Type B	No involvement of the ascending Ao

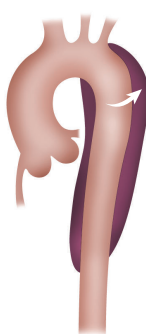
DEBAKEY CLASSIFICATION

Type I	Ascending Ao → extends at least to the aortic arch (± descending Ao)
Type II	Confined to the ascending Ao
Type III	Confined to the descending Ao



Type A Ao dissection

Involvement of the ascending Ao
(Surgical management)



Type B Ao dissection

No involvement of the ascending Ao
(Initially medical treatment)

RISK FACTORS

➤ AORTIC STRESS	DEGENERATION OF THE MEDIA
<ul style="list-style-type: none"> • Aortic aneurysm • Aortic valve disease • HTN • CoA • Recent aortic intervention • Trauma / Deceleration • Pheochromocytoma • Cocaine • Weightlifting • Penetrating ulcer • Infectious aortitis 	<ul style="list-style-type: none"> ➤ metalloproteinases; ↘ elastic fibers; ➤ proteoglycans <ul style="list-style-type: none"> • Degenerative / Atherosclerotic • Genetic: Marfan; Ehlers-Danlos type IV; Bicuspid aortic valve; Turner; Loeys-Dietz; Familial thoracic aortic aneurysm and dissection • Vasculitis: Takayasu; Giant cell arteritis; Behçet • Other: Pregnancy; Polycystic kidneys; Chronic corticosteroid therapy

PRESENTATION: Acute - severe - tearing pain; Retrosternal pain (type A) or back pain (type B)

- **Target organ ischemia:** Myocardial infarction; Stroke - TIA; Spinal cord ischemia (paraplegia / paraparesis) or mesenteric or renal or lower limbs; Ischemic neuropathy
- **Hemorrhagic:** Tamponade; Hemothorax; Hemomediastinum; Aortopulmonary or aorto-enteric or aorto-esophageal fistula
- **Aortic regurgitation:** Mechanisms: **A)** Aortic root dilatation (malcoaptation); **B)** Dissection involving a leaflet implantation site (leaflet prolapse); **C)** Transvalvular prolapse of the dissection flap; **D)** Underlying AR (bicuspid aortic valve)

CLINICAL FEATURES: Hypotension or Normotension or Hypertension (**measure BP in both arms**); Absent pulses (evaluate pulses in all extremities); **AR murmur**; Signs of tamponade; Neurological deficits; Abdominal signs

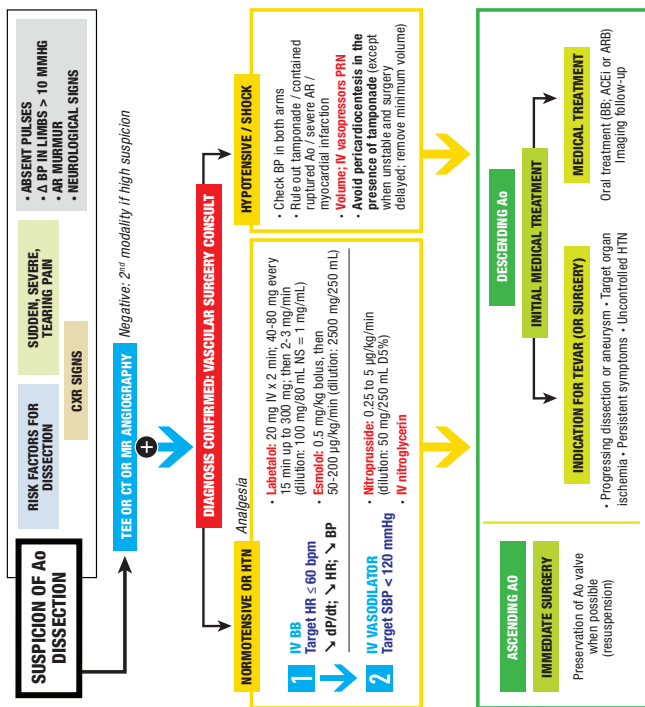
TEE: Dissection flap separating the true lumen and the false lumen (with independent movement); two flows on either side of the dissection flap on color Doppler; thrombus in the false lumen; look for the entry site and/or exit site of the dissection; pericardial effusion; myocardial ischemia (RWMA); AR; coronary ostia

	TRUE LUMEN	FALSE LUMEN
Size	True < False	False > True
Pulsation	Systolic expansion	Systolic compression
Direction of flow	Anterograde (systolic)	Retrograde or ↘ Anterograde systolic flow
Thrombus	Rare	Common
Contrast agent	Rapid opacification	Delayed opacification

CXR

- Aortic shadow** abnormal and enlarged
- Large mediastinum:** AP CXR → **> 8 cm at the carina**
- Calcium sign:** separation between calcification of the aortic intima and the lateral wall of the aortic knob **> 10 mm**
- Pleural effusion** (inflammatory reaction or hemothorax)
- Deviation of the trachea** towards the right (or deviation of the esophagus - NGT)
- Pulmonary edema** (AR)

PREOPERATIVE CORONARY ANGIOGRAPHY: it is reasonable not to perform coronary angiography in acute aortic syndrome, which constitutes a surgical emergency (class IIa recommendation)



08

POSTOPERATIVE COMPLICATIONS: Aneurysm formation (at the site of dissection or at the site of anastomosis or elsewhere); Recurrent dissection; Graft dehiscence; Pseudoaneurysm; AR; Infection; Progression of false lumen

FOLLOW-UP BY CT ANGIOGRAPHY OR MR ANGIOGRAPHY: 1-3-6-12-18-24 months; **+**
then annually

- **Type B aortic dissection:** TEVAR or surgical repair if aneurysm > 55-60 mm or > 4 mm/year growth or target organ ischemia or recurrent pain

AVOID ISOMETRIC EXERCISES; CONTROL BP

SPONTANEOUS INTRAMURAL HEMATOMA

Medial tear with bleeding inside the media, but absence of communication with the aortic lumen (absence of false lumen)

- Can propagate in an antegrade or retrograde fashion
- **May have an identical clinical presentation to that of aortic dissection**

IMAGING: Intramural thrombus; Enlarged wall **> 5 mm** (crescent-shaped or circular); Absence of flow (contrast) in wall **+**

COURSE: Resolution or stabilization or aneurysm formation or progression to aortic dissection or aortic rupture

MANAGEMENT: Similar to aortic dissection (for corresponding segment)

- Ascending Ao** → urgent surgery
- Descending Ao** → initial medical treatment; Indication for TEVAR (or surgery) according to aortic diameter or persistent symptoms or progression or compromise of branches (with ischemia)

PENETRATING ATHEROSCLEROTIC ULCER

Penetration of the aortic wall by an atherosclerotic ulcer (± secondary intramural hematoma); descending aorta in the majority of cases

COMPLICATIONS: Aortic dissection; Aortic rupture; Distal embolism (thrombus or cholesterol crystals); Aneurysm

MANAGEMENT

- Ascending Ao** → Surgery should be considered
- Descending Ao** → Initial medical treatment; Indication for TEVAR (or surgery) according to aortic diameter or persistent symptoms or progression or deteriorating associated intramural hematoma

8.3/ ABDOMINAL AORTIC ANEURYSM (AAA)

ANEURYSM: Abdominal Ao diameter > 30 mm

- Predominantly occurs in the infrarenal aorta
- Degeneration of the media (↗ metalloproteinases)
- **Risk factors:** Smoking; Family history; Age; Male gender; COPD; dyslipidemia; HTN

PRESENTATION: Asymptomatic; Embolism; Rapid expansion; Pain; Compression or erosion of adjacent structures; Rupture

ABDOMINAL ULTRASOUND: High sensitivity and specificity

- **Screening:** Male, 65 to 74 years with history of smoking; Male ≥ 60 years with family history of AAA

MANAGEMENT: Smoking cessation; treatment of HTN - dyslipidemia - DM; Surveillance of AAA

AAA REPAIR: Surgical or Percutaneous (EVAR) in a patient with **life expectancy > 2 years** +

MANAGEMENT – ABDOMINAL AORTIC ANEURYSM	
Indication for aneurysm repair (EVAR or open surgery)	<ul style="list-style-type: none"> • ≥ 55 mm or • Symptoms (pain) or • Progression > 10 mm per year (> 5 mm over 6 months) or • Infectious or inflammatory
AAA 30-39 mm	Surveillance every 3 years (progression ≈ 3 mm per year)
AAA 40-44 mm	Surveillance every 2 years
AAA > 45 mm	Surveillance every year

EVAR: endovascular AAA repair (for infra-renal AAA); anatomical suitability \rightarrow proximal aortic neck (segment between the lowest renal artery and the proximal extent of the aneurysm) > 10 -15 mm of length (and < 32 mm in diameter); adequate vascular access required

★ **EVAR and ★ DREAM:** surgical versus endovascular AAA repair; \searrow operative mortality with EVAR; **similar long term mortality;** \nearrow **reintervention with EVAR** +

SURGICAL AAA REPAIR SHOULD BE PREFERRED: anatomical criteria for EVAR not met or when regular long-term surveillance is impossible

- **Regular long-term surveillance following EVAR:** CT angiography or MR angiography at 1 month - 6 months - then annually; look for endoleakage, stent position, stability and exclusion of the aneurysm sac, stent fracture
- **Late complications of surgery:** para-anastomotic aneurysm; graft infection; graft-enteric fistula; imaging every 5 years

PATIENTS NOT CANDIDATES FOR SURGERY: significant comorbidities \rightarrow no benefit of EVAR on long term survival (★ EVAR 2)

8.4/ OTHER AORTIC DISEASES

AORTIC ATHEROSCLEROTIC PLAQUE

COMPLEX PLAQUE: Plaque thickness ≥ 4 mm or mobile / pedunculated debris (= thrombus) or ulceration +

- \nearrow embolic risk
- **Site:** particularly in the distal aortic arch and descending aorta

EMBOLISM: spontaneous or iatrogenic (post-intervention)

- **Thrombus (thromboembolism):** thrombus forms on an unstable plaque then embolizes to a medium-to-large artery (stroke; TIA; leg ischemia; renal or splenic infarction; mesenteric ischemia)
 - Consider anticoagulation if complex plaque in aortic arch with stroke / TIA (class IIb)
- **Cholesterol crystals (atheroembolism):** crystal emboli to small arterioles ("blue toe"; retinal ischemia / Hollenhorst plaques; Amaurosis fugax; TIA; Confusion; ARF; HTN; *Livedo reticularis*; Petechiae; Purpura; Intestinal ischemia; Pancreatitis)
 - **Hypocomplementemia; Eosinophilia**
 - **Consider endarterectomy or stent** in the presence of an identified source of embolism and recurrent atheroembolism

MANAGEMENT: Secondary prevention; ASA - Statin - control HTN / DM; smoking cessation

GENETIC AORTIC SYNDROMES

SYNDROME	DETAILS	FOLLOW-UP	MANAGEMENT
Marfan	<ul style="list-style-type: none"> FBN1 mutation Dilatation of aortic root (annulo-aortic ectasia) and ascending Ao; Type A dissection Ghent diagnostic criteria ▶▶▶ - Chapter 7 	<ul style="list-style-type: none"> TTE at diagnosis and after 6 months (stability) then every 6-12 months Follow-up by imaging of the entire aorta following repair of the ascending Ao 	<ul style="list-style-type: none"> BB; Losartan Surgery: A) > 50 mm; B) Progression > 5 mm/y; C) Family history of dissection < 50 mm; D) Significant AR Desire for pregnancy: surgery if ≥ 40 mm
Løeys-Dietz	<ul style="list-style-type: none"> Autosomal dominant TGFB1 or 2 mutation Tortuositities / aneurysms / artery dissection Hypertelorism; Cleft palate or bifid uvula Aneurysm of the aortic root; Aortic dissection 	<ul style="list-style-type: none"> Imaging of the entire aorta at diagnosis and after 6 months (stability) Annual MRI of the cerebrovascular circulation and as far as the pelvis 	<ul style="list-style-type: none"> Surgery if ascending Ao ≥ 42 mm (TEE; inner diameter) or ≥ 44 mm (CT or MRI; outer diameter)
Ehlers-Danlos Type IV	<ul style="list-style-type: none"> Autosomal dominant (COL3A1) Risk of artery rupture (including thoracic and abdominal aorta) Risk of rupture of the uterus / intestine 		<ul style="list-style-type: none"> Role of prophylactic repair remains uncertain (friable tissues) Follow-up by imaging
Turner	<ul style="list-style-type: none"> 45, X Small stature; Ovarian insufficiency Bicuspid aortic valve (20%); CoA (10%); Ao aneurysm; Ao dissection 	<ul style="list-style-type: none"> Look for risk factors of aortic dissection (bicuspid aortic valve / CoA / dilatation of thoracic Ao / HTN) In the presence of risk factors: annual TTE Otherwise: TTE every 3-5 years 	<ul style="list-style-type: none"> Surgery if maximum Ao area (cm²) / patient's height (m) > 10 Surgery if diameter > 25 mm/m²
Non-syndromic familial thoracic aortic aneurysm and dissection	<ul style="list-style-type: none"> Non-syndromic Autosomal dominant Variable penetrance Genes identified: TGFB1 and 2; ACTA2; MYH11; MYLK; PRKG1 	<ul style="list-style-type: none"> Family screening: 1st degree relatives of patients with unexplained dissection or aneurysm Genetic testing if several family members are affected 	<ul style="list-style-type: none"> TGFB1 mutation: similar management to that of Løeys-Dietz

VASCULITIS WITH AORTIC INVOLVEMENT

Destruction of vessels (inflammation; ↗ metalloproteinases; granulomas)

Takayasu	<ul style="list-style-type: none"> • Vasculitis of the aorta and its branches (stenosis and/or aneurysm) • Diagnostic criteria: < 40 years; Claudication (upper limbs or lower limbs); ↘ Brachial pulse; Aortic or subclavian murmur; sBP Difference > 10 mmHg arms; Stenosis of the Ao or its branches (CT angiography or MR angiography) • Treatment: Prednisone 50 mg; MTX; Azathioprine; Anti-TNFalpha
Giant cell arteritis (temporal arteritis)	<ul style="list-style-type: none"> • Vasculitis of the aorta and its branches • Diagnostic criteria: > 50 years; <i>de novo</i> headache; tenderness over temporal artery (or ↘ pulse); ↗ ESR (> 50 mm/h); Positive biopsy • Constitutional symptoms; Claudication of the jaw; Claudication of upper limbs; Visual symptoms; PMR; Aortic aneurysm / dissection • Treatment: Prednisone 50 mg
Behçet	<ul style="list-style-type: none"> • Diagnostic criteria: Mouth ulcers; Genital ulcers; Uveitis or retinal vasculitis; Erythema nodosum; Pseudofolliculitis; Pathergy • Arterial involvement: destruction of the media; aneurysm ± rupture (any artery can be affected)
Ankylosing spondylitis	<ul style="list-style-type: none"> • HLAB27+ • Diagnostic criteria: < 40 years; Low back pain; Morning stiffness; Slow progression; Improvement with exercise • AR; Dilatation of the aortic root

TRAUMATIC AORTIC RUPTURE

Predominantly involves the **aortic isthmus** (deceleration injury)

BP in arms > BP in legs; radiofemoral delay; interscapular murmur

CXR: widened mediastinum; displaced nasogastric tube (hematoma); Dilatation of aortic arch / descending aorta; pleural effusion

MANAGEMENT: TEVAR if suitable anatomy (or open surgery)

INFECTIOUS AORTITIS

Contiguous invasion or septic embolism (endocarditis) or hematogenous spread

SITE: on a pre-existing aortic lesion (aneurysm; atherosclerotic plaque; site of iatrogenic injury); predominantly involves the infrarenal aorta

MICROORGANISMS: *S. aureus*; *Salmonella*; Streptococcus; *E. coli*; *Neisseria*; Fungi; TB; Syphilitic aortitis (10-25 years post-infection)

COMPLICATIONS: sacular aneurysm; fistula; pseudo-aneurysm; rupture

8.5/ PERIPHERAL ARTERY DISEASE

PAD: cardiovascular risk equivalent to that of CAD

➤ **5-year mortality:** 10-15% (75% from cardiovascular causes)

RISK FACTORS: Smoking; DM; HTN; Dyslipidemia; Age; CRF; Chronic inflammation

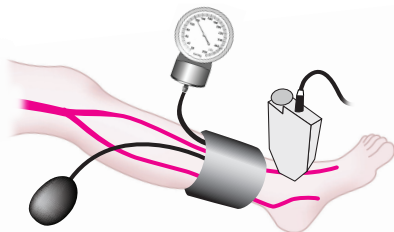
PRESENTATION: Asymptomatic; Intermittent claudication; Critical limb ischemia

CLINICAL FEATURES: ↘ pulse; murmur; pallor on elevation; ↗ erythema of limb in dependent position; coldness; muscle atrophy; hair loss; onychodystrophy; skin fissures; ulcers; devitalization - gangrene

FONTAINE CLASSIFICATION	
I	Asymptomatic
II	Intermittent claudication
IIa	Claudication > 200 m
IIb	Claudication < 200 m
III	Rest pain / night pain
IV	Ulcer / Gangrene

DDX: vasculitis (thromboangiitis obliterans; Takayasu; giant cell arteritis); CoA; fibromuscular dysplasia; external compression; radiotherapy; neurogenic claudication (lumbosacral radiculopathy); arthritis; myositis; venous insufficiency; popliteal artery entrapment syndrome

ANKLE-BRACHIAL INDEX



ABI ≤ 0.90	ABI 0.91 - 0.99	ABI 1.0 - 1.4	ABI > 1.4
Abnormal	Gray zone	Normal	Calcified noncompressible artery
<ul style="list-style-type: none"> Mild: 0.8-0.9 Moderate: 0.5-0.8 Severe: < 0.5 	ABI on exercise if persistent suspicion of PAD: diagnosis of vascular claudication if ABI ↘ by > 20-25 %		DM / CRF / Age → Use toe-brachial index (diagnostic if < 0.7)

ABI: ratio of SBP in ankle (posterior tibial artery or dorsalis pedis artery) / brachial artery

INDICATION FOR ABI: suspicion of PAD in the leg with:

- Suspected claudication; Poor wound healing; ≥ 50 years + [DM or Smoking]; ≥ 65 years; intermediate Framingham score

OTHER EXAMINATIONS: segmental BP measurements; Doppler US; MR angiography; CT angiography; Angiography

MANAGEMENT

MANAGEMENT OF RISK FACTORS: Smoking cessation; Statin; Treatment of DM (HbA1c < 7%); Control of BP; ACE inhibitors (★ HOPE)

ASA: ↘ mortality - stroke - myocardial infarction (★ Antithrombotic Trialists' Collaboration)

➤ **Indications**

- Symptomatic patient (claudication; critical limb ischemia; history of revascularization; history of amputation) (class I recommendation)
- Asymptomatic patient with ABI ≤ 0.90 (class IIa recommendation); limited evidence

➤ **Clopidogrel as alternative treatment:** superior to ASA in ★ CAPRIE; marginal benefit of ASA and Clopidogrel combination in ★ CHARISMA

SUPERVISED EXERCISE PROGRAM: 30-45 min; 3 x / week ; > 12 weeks; ↗ exercise capacity

CILOSTAZOL (100 MG PO BID): phosphodiesterase-3 inhibitor; ↘ platelet aggregation; direct arterial vasodilator; contraindicated in the presence of heart failure; beware of drug interactions

PENTOXIFYLLINE (400 MG PO TID): phosphodiesterase inhibitor; ↘ blood viscosity; ↗ erythrocyte deformability; marginal efficacy

REVASCULARIZATION: Indications → **A)** Symptoms refractory to medical treatment with impaired quality of life; **B)** Critical limb ischemia

Aorto-iliac	<ul style="list-style-type: none"> First-line endovascular revascularization (with stent) (TASC II type A - B - C) Surgical revascularization: aortofemoral bypass graft with Dacron or PTFE prosthesis; femorofemoral bypass graft; axillofemoral bypass graft 	
Femoro-popliteal	<ul style="list-style-type: none"> First-line endovascular revascularization (TASC II type A - B - C) Stenting for intermediate length (TASC type II B) Surgical revascularization: femoropopliteal bypass graft preferably with autologous venous conduit (or PTFE prosthesis) 	
Infra-popliteal (below the knee)	<ul style="list-style-type: none"> Revascularization in the presence of persistent critical limb ischemia despite proximal revascularization First-line endovascular revascularization Stenting if suboptimal result Surgical revascularization: femorotibial or femoroperoneal bypass graft (autologous venous conduit) 	

➤ **Mode of revascularization:** first-line endovascular treatment in most cases; decision by multidisciplinary team according to anatomy / durability / comorbidities / local expertise / patient preference

• **Percutaneous revascularization:** medium- and long-term patency decreased in the presence of a distal lesion / lesion > 10 cm / multiple lesions / poor distal runoff / DM / CRF

- **Surgical revascularization:** preferred in the case of disseminated disease or technically difficult endovascular revascularization or TASC II type D (\pm type C)
- **Regular surveillance:** for all patients post-revascularization; history - ABI - physical examination; \pm Doppler US (vein graft)
- **Antithrombotic therapy:** ASA for all patients; Clopidogrel 1 to 3 months post-stenting; consider Warfarin after bypass graft with vein graft

CRITICAL LIMB ISCHEMIA

DEFINITION: **A)** Ischemic pain at rest; **B)** Ischemic lesion (ulcer; gangrene)

- **sBP at ankle:** < 50 mmHg (rest pain) or < 70 mmHg (ischemic lesion)

ONE-YEAR MORTALITY: 25 %

MANAGEMENT: **A)** Analgesia; **B)** Urgent revascularization if tissues are still viable (endovascular if technically feasible); **C)** Amputation if tissues are devitalized; **D)** Secondary prevention - wound care - adjusted shoes - treatment of infectious complications

- ★ **BASIL:** revascularization by infrainguinal venous bypass graft similar to endovascular revascularization; ↘ reintervention with bypass graft; ↘ **mortality with bypass graft in patients surviving > 2 years**

ACUTE LIMB ISCHEMIA

MECHANISM: embolism (cardiac; Ao; peripheral arteries); thrombosis *in situ*; thromboembolism from a popliteal artery aneurysm (repair of aneurysm as primary prevention if > 20 mm); thrombosis of infrainguinal bypass graft; trauma; dissection; thrombophilia - hyperviscosity; *phlegmasia cerulea dolens*; iatrogenic (endovascular procedure; IABP; extracorporeal cardiac mechanical support)

PRESENTATION: Pain; Coldness; Pallor; Loss of pulse (Doppler PRN); Paresthesia / Sensory deficit; Weakness / Paralysis

MANAGEMENT: Medical emergency; **A)** IV Heparin; **B)** Percutaneous thromboembolectomy and/or direct intraarterial thrombolysis (first-line); **C)** Surgical revascularization (second-line)

ATHEROSCLEROSIS OF THE ARMS

Innominate / subclavian artery stenosis

SUBCLAVIAN STEAL SYNDROME: claudication of the arm; reversal of flow of the vertebral artery (vertigo; syncope; diplopia; dysarthria; ataxia) or of a mammary bypass graft (angina) to perfuse the arm

DETECTION: BP difference in arms \geq 10 mmHg

TREATMENT: endovascular or surgical revascularization

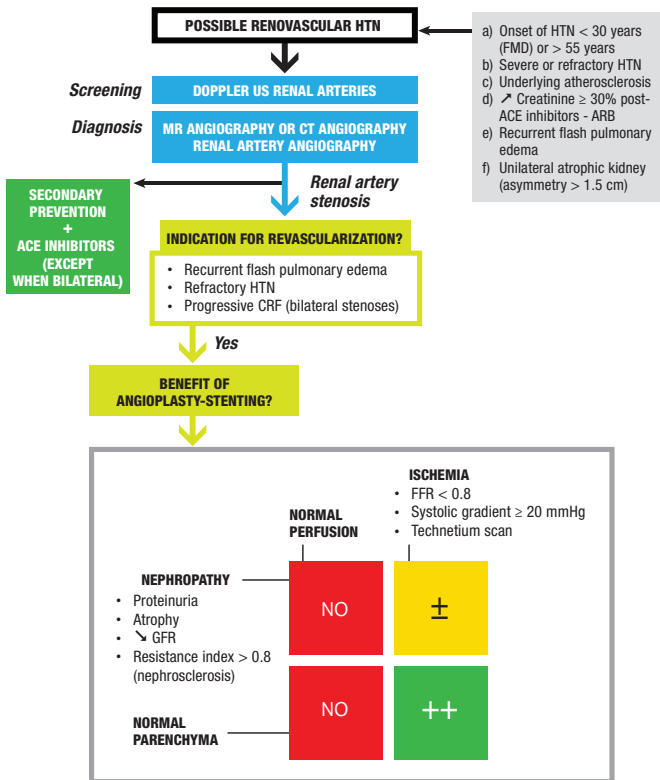
8.6/ ATHEROSCLEROTIC RENOVASCULAR DISEASE

↓ Renal perfusion → activation of renin-angiotensin-aldosterone system → peripheral vasoconstriction + salt and water retention → HTN

BILATERAL RENAL ARTERY STENOSIS (OR FUNCTIONAL SOLITARY KIDNEY): ↑ BP (renin-angiotensin-aldosterone system) with salt and water retention in the absence of compensatory sodium excretion → flash pulmonary edema

CONSEQUENCES: Asymptomatic; HTN; Flash pulmonary edema - Diastolic dysfunction; Progressive deterioration of renal function (ischemic nephropathy; hypertensive nephropathy in contralateral kidney + proteinuria)

MANAGEMENT



STUDY: no benefit with stenting in ★ CORAL

8.7/ CEREBROVASCULAR DISEASE

ETIOLOGIES – MECHANISMS

HEMORRHAGIC STROKE (20%)

INTRACEREBRAL HEMORRHAGE

RISK FACTORS: HTN; Trauma; Bleeding diathesis; Amyloid angiopathy; Vascular malformation; Tumor; Drugs

SUBARACHNOID HEMORRHAGE

- Ruptured aneurysm
- Explosive headache
- Blood in CSF

ISCHEMIC STROKE (80%)

ATHEROTHROMBOTIC (LARGE VESSELS)

- Intracranial or extracranial vessels
- Thrombosis *in situ* or Artery → artery embolism or Hypoperfusion
- ± Preceded by TIA in the same territory

CARDIOEMBOLIC

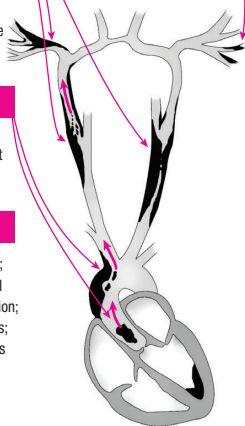
- Sudden onset
- Maximum deficit at onset
- Multiple territories

OTHER

Dissection; Thrombophilia; Hyperviscosity; Sickle-cell anemia; Systemic hypoperfusion; Arteritis; Vasospasm; Drugs; Cerebral venous thrombosis

LACUNAR (SMALL PENETRATING VESSELS)

- Lipohyalinosis (HTN; DM)
- Pure motor; Pure sensory; Hemiparesis / Ataxia; Dysarthria / Clumsy hand



TRANSIENT ISCHEMIC ATTACK (TIA)

TIA: transient episode (often < 1 h) of neurological dysfunction (focal cerebral or retinal or spinal ischemia) **in the absence of CNS infarction / permanent CNS injury**

ASSESSMENT: MRI (diffusion-weighted images - DWI) or brain CT scan; noninvasive imaging of head and neck vessels (carotid Doppler; CT angiography; MR angiography); ECG; TTE; ± TEE (cryptogenic TIA; suspicion of cardioembolic TIA); Holter; ± Evaluation of intracranial arteries (CT angiography or MR angiography or angiography or transcranial Doppler)

- **Evaluation of hereditary thrombophilia:** thrombophilia associated with venous >>> arterial thromboses; consider in the presence of cryptogenic TIA or suspected antiphospholipid syndrome (miscarriages; venous thrombosis; *livedo reticularis*) or personal or family history of systemic thrombosis

- **Look for:** protein C or S or antithrombin III deficiency; Leiden factor V; prothrombin mutation G20210A; lupus anticoagulant; anticardiolipin antibody

EVALUATION OF THE SHORT-TERM RISK OF STROKE

ABCD ² SCORE		
≥ 60 years	1 point	48-hour stroke risk 0-1: 0 % 2-3: 1 % 4-5: 4 % 6-7: 8 %
BP ≥ 140/90	1 point	
Dysphasia without weakness or Unilateral weakness	1 point 2 points	
Diabetes	1 point	
Duration 0-59 min Duration ≥ 60 min	1 point 2 points	

Rothwell OM, Giles MF, Flossmann E, et al. *Lancet*. 2005; 366: 29-36.
Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. *Lancet*. 2007; 369: 283-92.

CARDIOEMBOLIC SOURCE

ASSESSMENT: ECG; 24-hour monitor / Holter; TTE; TEE

- **Additional ambulatory electrocardiographic monitoring** beyond 24-hour for subclinical AF detection if cardioembolic TIA suspected (★ EMBRACE; ★ CRYSTAL-AF)

HIGH CARDIOEMBOLIC RISK	POTENTIAL CARDIOEMBOLIC RISK
<ul style="list-style-type: none"> LA (LAA) or LV thrombus AF - Flutter Recent MI (< 1 month) Rheumatic MS Prosthetic valve Severe LV dysfunction Infective endocarditis Noninfective endocarditis (Libman-Sacks; Antiphospholipid syndrome; Nonbacterial thrombotic endocarditis) Myxoma - Fibroelastoma ASD or VSD 	<ul style="list-style-type: none"> Complex atherosclerosis of the aorta Aortic valve disease Mitral annular calcification MVP PFO Atrial septal aneurysm LV aneurysm without thrombus Spontaneous echo contrast in LA Regional wall motion abnormality HCM LV noncompaction

ISCHEMIC STROKE

NIH STROKE SCALE (NIHSS): QUANTIFICATION OF NEUROLOGICAL IMPAIRMENT	
Level of consciousness	0 - Alert; 1 - Drowsy; 2 - Stuporous; 3 - Comatose
Orientation (2 questions)	0 - 2/2; 1 - 1/2; 2 - 0/2
Response to 2 commands	0 - 2/2; 1 - 1/2; 2 - 0/2
Gaze	0 - Normal lateral eye movements 1 - Partial gaze palsy 2 - Complete palsy
Visual fields	0 - No visual loss 1 - Partial hemianopia 2 - Complete hemianopia 3 - Bilateral hemianopia

Facial palsy	0 - Normal 1 - Minor paralysis 2 - Partial paralysis 3 - Complete paralysis
A) Motor function - left arm B) Motor function - right arm	0 - No drift 1 - Drift in 5 s 2 - Some effort against gravity; limb falls in 10 s 3 - No effort against gravity 4 - No movement
A) Motor function - left leg B) Motor function - right leg	0 - No drift 1 - Drift in 5 s 2 - Some effort against gravity; limb falls in 10 s 3 - No effort against gravity 4 - No movement
Ataxia	0 - Absent 1 - Present in one limb 2 - Present in two limbs
Sensory	0 - Normal 1 - Mild-to-moderate sensory loss 2 - Severe to total sensory loss
Language	0 - No aphasia; normal 1 - Mild-to-moderate aphasia 2 - Severe aphasia 3 - Mute, global aphasia
Dysarthria	0 - Normal 1 - Mild-to-moderate dysarthria 2 - Severe dysarthria
Extinction and Neglect	0 - No abnormality 1 - Visual, tactile, auditory, spatial, or personal inattention or extinction (1 sensory modality) 2 - Profound hemi-inattention or extinction to more than one modality

IMMEDIATE MANAGEMENT: ABC; Cardiac monitor (> 24 h); IV line; O₂ (if SaO₂ < 94%); Blood glucose; NPO

EXAMINATIONS: Unenhanced brain CT scan; Blood glucose; ECG; Electrolytes; Renal function; CBC; PT-aPTT; Troponin; ± Lumbar puncture (if suspicion of SAH and in the absence of bleeding on CT scan); ± EEG (rule out seizures)

DDX: Conversion; Hypertensive encephalopathy; Hypoglycemia; Complicated migraine; Seizures; Poisoning

INTRAVENOUS THROMBOLYSIS: rtPA 0.9 mg/kg IV (max 90 mg) over 60 min (10% of dose as a bolus over 1 min)

- **★ NINDS rtPA Stroke Study:** < 3 h after onset of symptoms; improvement of neurological recovery at 3 months; similar mortality to that with placebo; cerebral hemorrhage in 6% of patients
 - **3 to 4.5 h of symptoms:** ★ ECASS-3; improvement of neurological recovery at 3 months
- **Post-thrombolysis:** intensive care; monitoring of neurological signs every 15-30 min for 6 h, then hourly for 24 h; Brain CT scan STAT if suspicion of intracranial hemorrhage; BP every 15-30 min for 6 h then hourly for 24 h; target BP < 180/105; repeat CT scan after 24 h

CANDIDATES FOR INTRAVENOUS THROMBOLYSIS	
< 3 h after onset of symptoms	3 to 4.5 h after onset of symptoms
<p>A) Ischemic stroke with measurable neurological deficit (not minor);</p> <p>B) Absence of improvement of neurological deficit;</p> <p>C) Caution in the presence of major neurological deficit (risk of hemorrhagic transformation);</p> <p>D) Absence of SAH;</p> <p>E) Absence of head injury or stroke < 3 months;</p> <p>F) Absence of myocardial infarction < 3 months (risk of myocardial rupture; relative contraindication);</p> <p>G) Absence of GI or urinary bleeding < 21 days;</p> <p>H) Absence of major surgery < 14 days;</p> <p>I) Absence of noncompressible arterial puncture < 7 days;</p> <p>J) Absence of history of intracranial hemorrhage;</p> <p>K) Absence of CNS neoplasm / AVM / intracranial aneurysm;</p> <p>L) Absence of recent intracranial or spinal surgery;</p> <p>M) BP < 185/110;</p> <p>N) Absence of active internal bleeding;</p> <p>O) INR < 1.7;</p> <p>P) DOAC: normal sensitive detection test or last dose > 48 h (with normal renal function);</p> <p>Q) Normal aPTT if heparin received < 48 h;</p> <p>R) Platelet count > 100,000 mm³;</p> <p>S) Blood glucose > 2.7 mmol/L;</p> <p>T) Absence of seizures with residual neurological impairment;</p> <p>U) Brain CT scan: absence of multilobar infarction (1/3 of a cerebral hemisphere)</p>	<p>Same criteria as for thrombolysis < 3 h of symptoms</p> <p style="text-align: center; font-size: 2em;">+</p> <p>Exclusion criteria:</p> <p>a) > 80 years</p> <p>b) Oral anticoagulants</p> <p>c) NIHSS > 25</p> <p>d) History of stroke + DM</p> <p>e) Ischemic lesion > 1/3 of the middle cerebral artery territory</p>

INTRAARTERIAL REVASCLARIZATION

- ★ **MR CLEAN:** stroke < 6 h + proximal occlusion in the anterior cerebral circulation; 89% treated with IV tPA before randomization; intraarterial thrombolysis and/or mechanical thrombectomy versus usual care; benefit on the functional outcomes
- ★ **ESCAPE:** stroke < 12 h + proximal intracranial occlusion in the anterior circulation; early thrombectomy associated with improved functional outcome and ↓ mortality

MANAGEMENT OF BP

- **BP > 220/120 mmHg:** 10-15% ↓ BP for 24 h (Nicardipine; Labetalol)
- **Thrombolysis considered:** target BP < 185/110
 - Labetalol 10-20 mg IV x 1-2 min (can be repeated once)
 - Nicardipine: 5 mg/h (titrate every 5-10 min up to 15 mg/h; when target BP has been achieved → 3 mg/h infusion)
- **Post-thrombolysis:** Labetalol 10 mg IV x 1-2 min (then every 10-20 min; max 300 mg) or Labetalol 10 mg IV then 2-8 mg/min infusion or Nicardipine (as above)
- **Post-stroke (long-term):** target BP < 140/90 (ACE inhibitors and/or diuretics); resume antihypertensives 24 h after stroke

ASA: 325 mg in < 48 h (> 24 h in the case of thrombolysed stroke); benefit on the morbidity - mortality

OTHER TREATMENTS: **A)** Thromboprophylaxis / sequential compression device; **B)** Detection of dysphagia (water swallow test); **C)** Target normothermia and normoxemia; **D)** Nutritional support; **E)** Insulin if blood glucose > 10.3 mmol/L (avoid hypoglycemia); **F)** Rehabilitation

SECONDARY PREVENTION

RISK FACTORS: ►►I Chapter 9; Treatment of HTN (from 24 h); Smoking cessation; Treatment of dyslipidemia (★ SPARCL); Treatment of DM; Moderate alcohol intake; Regular moderate physical exercise; Healthy weight; Balanced diet; Treat OSAHS

ANTIPLATELET THERAPY: indicated in a context of noncardioembolic TIA or ischemic stroke; ASA (50 to 325 mg daily) or ASA 25 mg / Dipyridamole 200 mg bid or Clopidogrel 75 mg daily

- **Evidence:** similar outcomes with Clopidogrel versus ASA / Dipyridamole (★ PROFESS); no benefit of long-term combination of Clopidogrel and ASA (★ MATCH); ↘ adverse events with ASA / Dipyridamole versus ASA (★ ESPS-2; ★ ESPRIT)

ATRIAL FIBRILLATION: Warfarin (★ EAFIT) or DOAC for secondary prevention

- **Initiation of A/C in acute stroke:** according to the severity of the stroke (risk of hemorrhagic transformation); anticoagulant therapy initiated < 14 days in ★ EAFIT; wait 72 h for small stroke or 1 week for moderate stroke or 2 weeks for large stroke; no benefit of Heparin bridge
- **WATCHMAN:** LAA occlusion device; ★ PROTECT AF (noninferior to warfarin); consider when anticoagulation is contraindicated

LVEF ≤ 35 %: no evidence in support of warfarin for secondary prevention; Warfarin or ASA or Clopidogrel or ASA / Dipyridamole

RHEUMATIC MITRAL STENOSIS: Warfarin

NONRHEUMATIC VALVULAR HEART DISEASE: Aortic or mitral valve disease or mitral annular calcification or MVP; Antiplatelet therapy (IIb; C)

PFO: controversial subject; ►►I Chapter 7 - Congenital heart disease

THROMBOPHILIA: associated with venous >>> arterial thromboses; anticoagulation if concomitant DVT; Antiplatelet therapy or anticoagulation in the absence of DVT or an identifiable cause of stroke

- **Antiphospholipid syndrome:** anticoagulation indicated

CAROTID ARTERY REVASCLARIZATION

SYMPTOMATIC CAROTID ARTERY STENOSIS: benefit of surgical revascularization compared to medical treatment (★ NASCET; ★ ECST; ★ VACS); NNT = 6

ASYMPTOMATIC CAROTID ARTERY STENOSIS: benefit of surgical revascularization in selected patients (★ ACAS and ★ ACST; studies conducted prior to the introduction of modern medical treatment); NNT = 33

ANGIOPLASTY-STENTING VERSUS ENDARTERECTOMY: comparable long-term outcomes (★ CREST; ★ SAPPHIRE)

- **Angioplasty-Stenting:** increased risk of periprocedural stroke compared to endarterectomy (particularly in patients > 70 years)
- **Prefer angioplasty-stenting:** anatomical / technical considerations (post-radiation; post-surgical; obesity; hostile neck; stenosis at different level); high operative risk - severe comorbidities
- **Dual antiplatelet therapy:** 4 weeks

REVASCLARIZATION IN THE PRESENCE OF MULTIPLE COMORBIDITIES: little evidence in favor of surgical or endovascular revascularization (NYHA III-IV; CCS III-IV; CAD ≥ 2 vessels or LMCA; LVEF ≤ 30%; recent myocardial infarction; severe lung disease; advanced CRF)

SYMPTOMATIC (< 6 MONTHS)			ASYMPTOMATIC
	Carotid artery stenosis: 50-69% (angiography)	Carotid artery stenosis: 70-99% (noninvasive imaging)	Carotid artery stenosis > 70%
Endarterectomy	I; B	I; A	IIa; A
	To be performed within 14 days of the neurological event unless contraindicated (IIa; B)		Mortality - perioperative stroke < 3%
	Mortality - perioperative stroke < 6% Life expectancy > 5 years		Life expectancy > 5 years
Angioplasty-Stenting	Alternative to surgery: I; B	Alternative to surgery: I; B	IIb; B (controversial)
	Mortality - perioperative stroke < 5%		

INTRACRANIAL HEMORRHAGE

MANAGEMENT: Intensive care; Neurosurgical assessment; Target normothermia; Target blood glucose < 10.3 mmol/L; Thromboprophylaxis (sequential compression device; IVC filter PRN); Phenytoin in the presence of seizures; \pm Continuous EEG monitoring

ANTICOAGULATION: Discontinue anticoagulation and antiplatelet therapy for more than 1-2 weeks and subsequently reassess the indication; weigh up the thromboembolic risk against the bleeding risk (high in cortical stroke secondary to amyloid angiopathy)

- **Reverse Warfarin: prothrombin complex concentrate** (Octaplex; Beriplex; Cofact; Proplex); complex of factors II - VII - IX - X; Target INR < 1.4
 - **Vitamin K:** 10 mg IV (max 1 mg/min)
 - **Fresh frozen plasma:** 8 units when prothrombin complex concentrate is not available

BLOOD PRESSURE: treat if SBP > 180 mmHg in the absence of intracranial hypertension; target BP < 160/90 (labetalol; nicardipine; esmolol; enalapril; hydralazine; nitroprusside; TNT)

CONTROL OF INTRACRANIAL HYPERTENSION: target cerebral perfusion pressure > 60 mmHg (MAP - ICP) and ICP < 20-25 mmHg; raise head of bed by 30°; analgesia; control of BP (target SBP < 180 mmHg and MAP < 130 mmHg, while maintaining adequate cerebral perfusion pressure); ventriculostomy (external CSF drainage); IV mannitol (target plasma osmolality: 300-310 mOsmol/kg); sedation; hyperventilation (PaCO₂: 30-35 mmHg); neuromuscular blockade; surgical evacuation of hematoma; barbiturate-induced coma

8.8/ PULMONARY EMBOLISM

RISK FACTORS: Age; Personal or family history of pulmonary embolism; Cancer; Trauma; Surgery; Immobilization; Pregnancy; Hormonal therapy; Oral contraceptive; Nephrotic syndrome; Chemotherapy

- **Thrombophilia:** Homozygous factor V Leiden; Homozygous prothrombin G20210A; Protein C deficiency; Protein S deficiency; Antiphospholipid syndrome / Lupus anticoagulant

PRESENTATION: Dyspnea; Pleuritic pain; Retrosternal chest pain; Cough; Hemoptysis; Paradoxical embolism; Syncope; Sudden death - Pulseless electrical activity

CLINICAL FEATURES: Tachypnea; Tachycardia; \pm Shock; \pm Cyanosis (R \rightarrow L shunt via PFO); \searrow SaO₂; Low-grade fever; JVD; Left parasternal heave; \nearrow P2; TR murmur; right S3 or S4; Pleural friction rub (pulmonary infarction); signs of DVT in leg (edema; erythema; heat; pain; difference between legs)

D-DIMERS: very sensitive but not specific

ECG: Sinus tachycardia; S1Q3T3; *de novo* RBBB; T wave inversion (V1 to V4; inferior leads); Q in III and aVF; Qr in V1; ST depression or ST elevation in V1-V4; right axis deviation; AF / Flutter

CXR: PA dilatation; Atelectasis; Elevation of the diaphragm; Pleural effusion

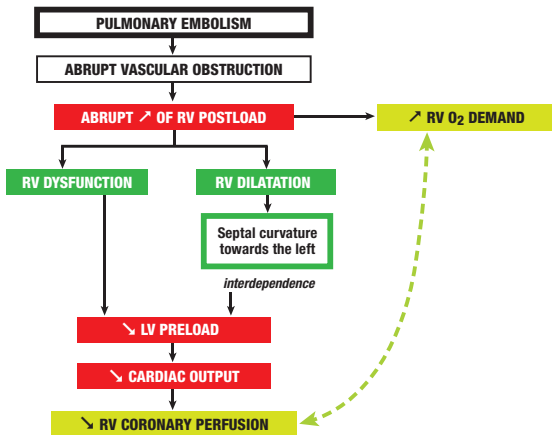
- > **Westermarck sign:** Segmental oligemia secondary to proximal arterial occlusion
- > **Hampton hump:** Triangular hyperdensity adherent to the pleura secondary to pulmonary infarction (consolidation with hemorrhage)

TTE: RV dilatation (↗ acute afterload); RV hypokinesia; PHT (non-preconditioned RV is unable to generate a mPAP > 40 mmHg); TR; shunt via PFO; thrombus-in-transit visible in right chambers / PA; septal curvature towards the LV; dilated and noncompliant IVC

- > **McConnell's sign:** hypokinesia of basal / mid RV free wall (preserved apex contractility) **+**

LEG ULTRASOUND: look for ↘ vein compressibility

CONSEQUENCES OF PULMONARY EMBOLISM

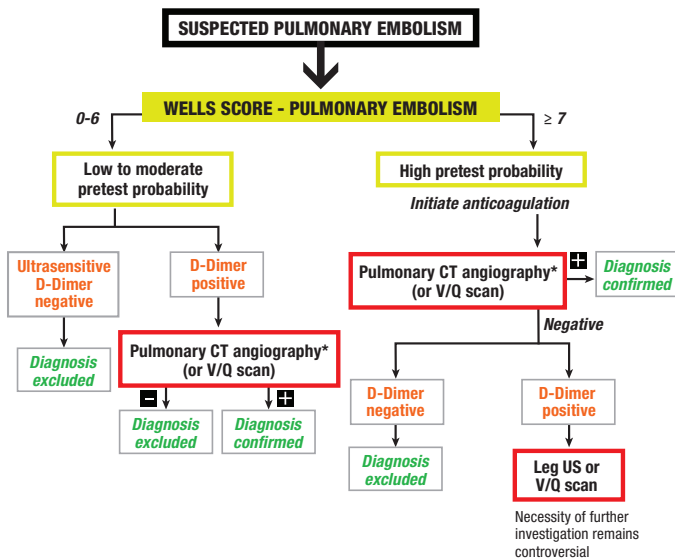


ASSESSMENT

WELLS CRITERIA – PRETEST PROBABILITY – DEEP VEIN THROMBOSIS		
Active cancer	1 point	<ul style="list-style-type: none"> • 0 point: low pretest probability • 1-2 points: moderate pretest probability • ≥ 3 points: high pretest probability
Paralysis or recent cast immobilization	1 point	
Bedridden > 3 days or surgery < 4 weeks	1 point	
Local vein tenderness	1 point	
Swelling of entire leg	1 point	
Difference between calves > 3 cm	1 point	
Pitting edema	1 point	
Superficial collateral vein	1 point	
Alternative diagnosis at least as likely	- 2 points	

WELLS CRITERIA – PRETEST PROBABILITY – PULMONARY EMBOLISM		
Signs or symptoms of DVT	3 points	<ul style="list-style-type: none"> • 0-1 point: low pretest probability (10%) • 2-6 points: moderate pretest probability (30%) • ≥ 7 points: high pretest probability (65%)
Alternative diagnosis is less likely	3 points	
HR > 100 bpm	1.5 points	
Immobilization or surgery < 4 weeks	1.5 points	
History of DVT or pulmonary embolism	1.5 points	
Hemoptysis	1 point	
Cancer (< 6 months or metastasis)	1 point	

Wells PS, Anderson DR, Bormanis J, et al, Lancet 1997; 350:1795
van Belle A, et al. JAMA 2006; 295:172

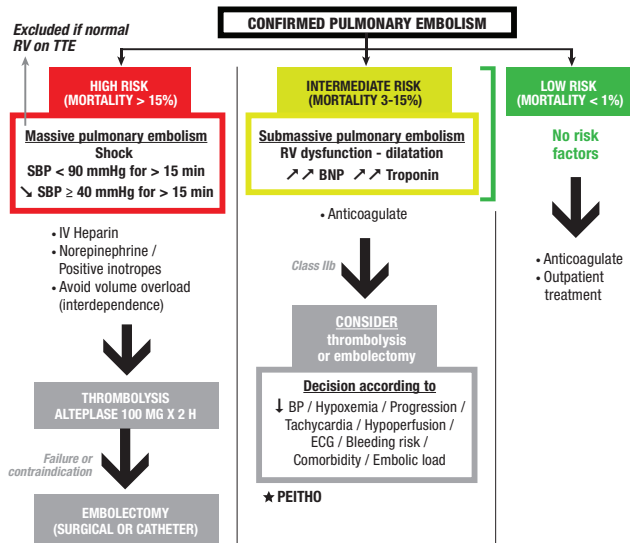


* Interpret according to:

A) Pretest probability

B) Site of thrombus (main PA or lobar or segmental versus subsegmental PA)

MANAGEMENT



- ★ **PEITHO**: PE with RV dysfunction and ↗ Troponin; Tenecteplase + Heparin vs Heparin;
 ↘ Haemodynamic decompensation; similar all-cause 7-day mortality; ↗ intracranial bleeding;
 ↗ major hemorrhage

Unfractionated heparin	<ul style="list-style-type: none"> • IV bolus: 80 IU/kg • IV infusion: 18 IU/kg/h (target aPTT 1.5-2.5 x control or 60-80 s) 	
Enoxaparin	• 1 mg/kg SC bid or 1.5 mg/kg qd	LMWH <ul style="list-style-type: none"> • Better bioavailability • More predictable effect • Avoid if GFR < 30 mL/min
Dalteparin	• 100 IU/kg SC bid or 200 IU/kg qd	
Tinzaparin	• 175 IU/kg SC bid	
Fondaparinux	<ul style="list-style-type: none"> • < 50 kg: 5 mg SC qd • 50-100 kg: 7.5 mg SC qd • > 100 kg: 10 mg SC qd 	<ul style="list-style-type: none"> • Indirect Xa inhibitor • Avoid if GFR < 30 mL/min
History of HIT	Argatroban or Bivalirudin or Lepirudin or Danaparoid	

WARFARIN: anticoagulant effect in 5 days

- **Initially procoagulant effect**: due to ↘ proteins C and S
- Overlapping of warfarin with Heparin ≥ 5 days (and ≥ 24 h with INR ≥ 2.0)

+

Provoked pulmonary embolism or proximal DVT (secondary to surgery; trauma; pregnancy; hormonal therapy)	Thromboembolism and active cancer	Idiopathic or recurrent pulmonary embolism (or proximal DVT)
Anticoagulation x 3 months	LMWH (★ CLOT) Continue in the presence of active cancer (warfarin as alternative)	Anticoagulation x ≥ 3 months and consider long-term treatment (according to balance between the risks of recurrence and bleeding)

DOAC IN ACUTE PHASE OF THROMBOEMBOLIC DISEASE: ★ EINSTEIN (Rivaroxaban 15 mg bid x 3 weeks then 20 mg qd); ★ AMPLIFY (Apixaban 10 mg bid x 7 days then 5 mg bid)

SECONDARY PREVENTION (after acute phase): Options → **A)** Warfarin; **B)** Rivaroxaban 20 mg qd (★ EINSTEIN-extension); **C)** Apixaban 2.5 mg bid (★ AMPLIFY-extension); **D)** Dabigatran 150 mg bid (★ RE-SONATE and ★ RE-MEDY); **E)** ASA 100 mg qd (★ ASPIRE and ★ WARFASA)

IVC FILTER: Indications → **A)** Bleeding / Contraindication to anticoagulation; **B)** Recurrent pulmonary embolism despite treatment (in the presence of a proximal thrombosis)

- ↘ Pulmonary embolism recurrence rate; ↗ DVT recurrence rate
- **Complications:** access site complication; recurrent DVT; IVC thrombosis; IVC perforation; migration; post-thrombotic syndrome
- Resume anticoagulation and **remove** the filter as soon as possible

INTRAVENOUS THROMBOLYSIS: ↘ **mortality in massive pulmonary embolism**

- **Alteplase 100 mg IV x 2 h** (without heparin); resume heparin without bolus at the end of thrombolysis if aPTT ≤ 80 s

CATHETER-ASSISTED THROMBUS REMOVAL

- **Indications:** Hemodynamic instability with → **A)** Contraindication to thrombolysis or **B)** Failure of thrombolysis (rescue)
- **Consider surgery** in the presence of mobile thrombus-in-transit in right chambers or thrombus-in-transit in PFO

LOCAL CATHETER THROMBOLYSIS FOR DVT: **A)** Extensive ilio-femoral thrombosis with low bleeding risk (including *phlegmasia cerulea dolens*); **B)** Progression of thrombus despite treatment; **C)** Extensive upper extremity DVT (subclavian and axillary veins)

- **Benefit:** ↘ risk of postthrombotic syndrome
- **Pharmacomechanical approach:** local thrombolysis combined with catheter thrombectomy \pm balloon venoplasty (\pm stent)

UPPER EXTREMITY DVT: Risk factors → central catheter; pacemaker; thoracic outlet syndrome (Paget-Schroetter disease); Cancer

- Risk of complications in the case of proximal DVT (starting at axillary vein)
- **Risk of PE:** 10 %
- **Anticoagulation:** ≥ 3 months
 - It is acceptable to observe upper extremity DVT **distal to the axillary vein**

POSTTHROMBOTIC SYNDROME: varicosities; hyperpigmentation; ulcers

- **Compression stockings:** 30-40 mmHg
- Consider angioplasty \pm stenting in the presence of iliac vein obstruction

THROMBOPROPHYLAXIS IN MEDICALLY HOSPITALIZED PATIENTS

- **Unfractionated heparin:** 5000 IU SC bid or tid
- **LMWH:** Enoxaparin 40 mg SC qd or Dalteparin 5000 U SC qd
- **Fondaparinux:** 2.5 mg SC qd (useful in patients with a history of HIT)
- **Intermittent pneumatic compression:** contraindication to anticoagulants or multiple risk factors (with anticoagulant)

8.9/ HEPARIN-INDUCED THROMBOCYTOPENIA (HIT)

TYPE 1 HIT: Benign form

TYPE 2 HEPARIN-INDUCED THROMBOCYTOPENIA

Immune form (IgG)

PATHOPHYSIOLOGY: Antibody directed against neoantigens on protein PF4 (protein released by activated platelets)

- Neoantigens are exposed following binding of PF4 with heparin → IgG binds simultaneously to the heparin-PF4 complex and to platelet Fc receptors → platelet activation with release of prothrombotic molecules → platelet consumption + intense thrombin production → multiple thromboses (venous or arterial)

5-10 days post-exposure to heparin (or earlier in the case of re-exposure < 3 months)

> 50% of platelets (compared to baseline count) or thrombosis beginning 5-10 days after the start of heparin

+

4 T SCORE			
	2 POINTS	1 POINT	0 POINT
Thrombo-cytopenia	> 50% decrease in platelet count and nadir \geq 20,000/ μ L and no surgery in past 3 days	<ul style="list-style-type: none"> > 50% decrease in platelet count and surgery in past 3 days or 30-50% decrease in platelet count or Nadir 10,000-20,000/μL 	<ul style="list-style-type: none"> < 30% decrease in platelet count or Nadir < 10,000/μL
"Timing" (post-exposure)	Day 5 to Day 10 (or \leq 1 day if prior heparin exposure within 30 days)	Uncertain interval (but probably between Day 5 and Day 10) or after Day 10 (or \leq 1 day if prior heparin exposure within 30-100 days)	Decrease in platelet count \leq Day 4 (no other heparin therapy during past 100 days)
Thrombosis	Confirmed new thrombosis; Skin necrosis at injection site; Anaphylactoid reaction to IV heparin bolus	Recurrent venous thrombosis while on anticoagulant therapy or suspected thrombosis or nonnecrotic skin lesions at injection site	None
Other causes	No alternative cause to explain thrombocytopenia	Possible alternative cause	Probable alternative cause (recent surgery; bacteremia; chemotherapy; drugs...)
<p>6-8 points: high probability (34%)</p> <p>4-5 points: intermediate probability (11%)</p> <p>0-3 points: low probability (0.9%)</p>			

Lo GK, Warkentin TE, Sigouin CS et al. *J Thromb Haemost.* 2006; 4: 759-65.

DIAGNOSTIC WORK-UP: to be performed in the case of intermediate to high probability (4 T score)

- **ELISA assay of anti-PF4 antibodies** (excellent NPV but low PPV)
- **Serotonin-release assay** (platelets containing labeled serotonin placed in contact with the patient's plasma and heparin); gold standard diagnostic test

PREVENTION: CBC every 2-3 days (starting on Day 5 of heparin therapy)

MANAGEMENT OF TYPE 2 HIT

- 1) Stop all forms of heparin
- 2) Argatroban or Bivalirudin or Fondaparinux or Danaparoid
- 3) Initiate Warfarin **once the thrombocytopenia has resolved** (with IV co-administration of a direct thrombin inhibitor; overlapping for ≥ 5 days; discontinue after achieving therapeutic INR for 2 days); anticoagulation ≥ 3 months if confirmed thrombosis
 - If the patient is treated with Warfarin at the time of HIT: reverse with vitamin K

8.10/ PULMONARY HYPERTENSION

PHT	GROUP 1–3–4–5 PHT	POSTCAPILLARY (GROUP 2)
mPAP ≥ 25 mmHg	mPAP ≥ 25 mmHg Wedge ≤ 15 mmHg	mPAP ≥ 25 mmHg and Wedge > 15 mmHg
		Isolated postcapillary: dPAP - Mean Wedge < 7 mmHg and/or PVR ≤ 3 WU
		With precapillary component: dPAP - Mean Wedge ≥ 7 mmHg and/or PVR > 3 WU

ETIOLOGIES

Group 1: Pulmonary arterial hypertension (PAH)	mPAP ≥ 25 mmHg; Wedge ≤ 15 mmHg; PVR ≥ 3 WU
	<ul style="list-style-type: none"> • Idiopathic PAH • Heritable PAH <ul style="list-style-type: none"> - BMPR2; ALK1; Endoglin; SMAD9; CAV1; KCNK3 mutation - Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu) • PAH secondary to drugs - toxins (Anorectics; Cocaine; Amphetamines) • PAH associated with <ul style="list-style-type: none"> - Collagen diseases <ul style="list-style-type: none"> ➤ Scleroderma - CREST; SLE; Mixed connective tissue disease; RA; Sjögren; Dermatomyositis - HIV - Portal hypertension (Cirrhosis) <ul style="list-style-type: none"> ➤ Liver transplantation contraindicated if mPAP ≥ 35 mmHg or PVR > 250 dyn \times s / cm^5 - Congenital heart disease (Shunt) <ul style="list-style-type: none"> ➤ VSD; Patent ductus arteriosus; ASD; Anomalous pulmonary venous return; AV canal defect; Complex congenital heart disease - Schistosomiasis

Group 1	<ul style="list-style-type: none"> • Pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis <ul style="list-style-type: none"> - Similar presentation to that of PAH - Suspect in the presence of pulmonary edema following administration of pulmonary artery vasodilators - Characteristic changes on pulmonary HDCT (subpleural thickened septal lines; centrilobular ground-glass opacities; lymphadenopathy)
Group 2: PHT secondary to left heart disease	mPAP \geq 25 mmHg; Wedge $>$ 15 mmHg <ul style="list-style-type: none"> • LV systolic dysfunction • LV diastolic dysfunction • Left-sided valvular heart disease • Pulmonary veins stenosis
Group 3: Pulmonary hypertension secondary to lung disease	<ul style="list-style-type: none"> • COPD • Interstitial lung disease • Mixed lung disease • Sleep-disordered breathing • Alveolar hypoventilation • High altitude
Group 4	<ul style="list-style-type: none"> • Thromboembolic pulmonary hypertension
Group 5: Uncertain mechanism	<ul style="list-style-type: none"> • Hematological disease: Myeloproliferative disease (Polycythemia vera; Essential thrombocythosis; CML); Splenectomy; Chronic hemolytic anemia (Sickle-cell anemia; Hereditary spherocytosis; Homozygous beta-thalassemia) • Systemic disease: Sarcoidosis; Langerhans cell histiocytosis; Lymphangioleiomyomatosis; Neurofibromatosis; Vasculitis • Metabolic disease: Glycogen storage disease; Gaucher; Thyroid disease • Other: Neoplastic obstruction; Fibrosing mediastinitis; Dialysis
Reversible causes of PHT secondary to \nearrow transpulmonary blood flow Exercise; Anemia; Pregnancy; Sepsis; Hyperthyroidism; Volume overload	

ASSESSMENT

PRESENTATION: Dyspnea on exertion; Fatigue; Retrosternal chest pain; Syncope; Palpitations; Leg edema; Ortner's syndrome (recurrent laryngeal nerve compression by dilated PA); Hemoptysis

CLINICAL FEATURES: Hypotension; Cold extremities; \pm Cyanosis; JVD (\nearrow A wave; \nearrow V wave); left parasternal heave; Pulmonary artery palpable in left second intercostal space; \nearrow P2; Ejection click / Systolic ejection murmur at pulmonary site; Holosystolic murmur (TR; \nearrow on inspiration); PR murmur (Graham-Steel); Right S3 and/or S4; Pulsatile liver; Anasarca

- > Look for signs of collagen disease (sclerodactyly; arthritis; telangiectasias; Raynaud; rash) and liver disease (spider naevi; testicular atrophy; palmar erythema); look for clubbing

ASSESSMENTS: HIV; ANA; RF; LFTs (\pm liver US); BNP; TSH; Thrombophilia screening (group 4)

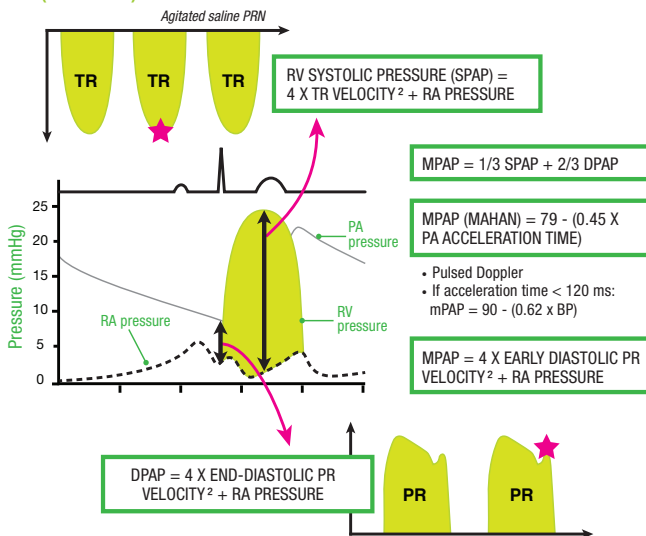
ECG: RAH; RVH; R axis deviation; T wave inversion in R precordial leads; RBBB; Atrial arrhythmias

CXR: central PA dilatation; RA-RV dilatation; pruning (loss) of the peripheral blood vessels (oligemia)

TTE: \nearrow PAP; RA and RV dilatation (RV / LV basal diameter ratio $>$ 1.0); PA dilatation ($>$ 25 mm); RVH; RV dysfunction (RIMP - S' - TAPSE - Strain); Curvature of the septum towards LV; Small left chambers; TR; Pericardial effusion; Look for shunt; Look for cause of PHT due to heart disease

- > **Screening: A)** Scleroderma: annually (+ DLCO / biomarkers); **B)** Sickle-cell anemia: annually

TTE (CONTINUED)



CARDIAC MRI: More favorable prognostic factors → Ejection volume > 25 mL/m² or RV end-diastolic volume < 84 mL/m² or LV end-diastolic volume > 40 mL/m²

PULMONARY ASSESSMENT: CXR; PFTs; Pulmonary high-resolution CT; Arterial blood gases; V/Q scan (± CT angiography / pulmonary angiography); Nocturnal saturimetry / Polysomnography

- **PFTs:** PAH associated with mild-to-moderate ↓ lung volumes and ↓ DLCO (40 to 80% of predicted)
- **Rule out thromboembolic PHT (Group 4) in all patients by V/Q scan** +

RIGHT/LEFT CATHETERIZATION

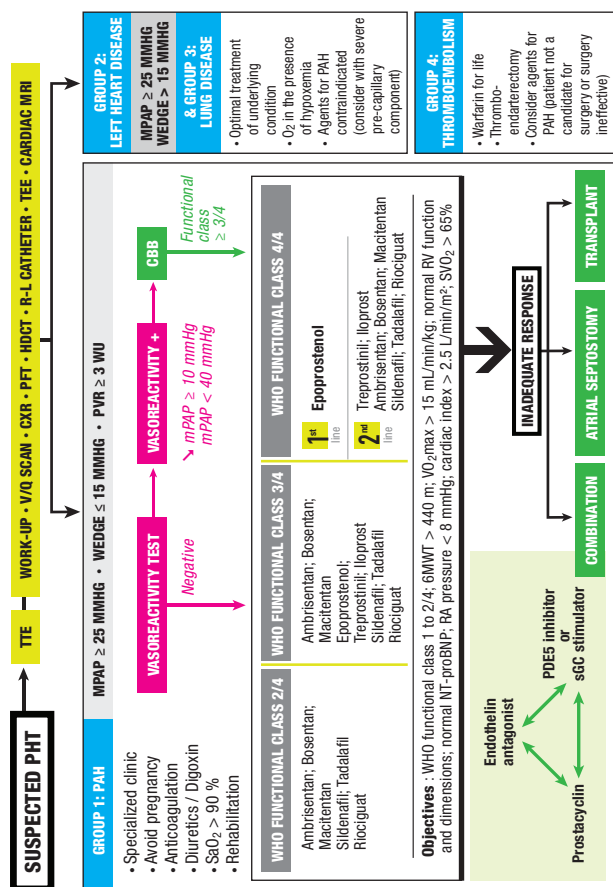
- **Look for a shunt** (oximetry run)
- **Wedge pressure** (end of expiration) ± LVEDP; 500 mL bolus PRN to reveal diastolic dysfunction
- **Cardiac output:** Thermodilution (in the absence of significant TR or low output state or shunt) or Fick
- **PVR (WU)** = mPAP - Wedge / Cardiac output
- **Diastolic pressure gradient** = dPAP - Mean Wedge
- **Vasoreactivity test** (Idiopathic PAH; Heritable PAH; Drug-induced PAH)
 - **Positive:** absolute ↓ of mPAP ≥ 10 mmHg (to mPAP < 40 mmHg) in the absence of ↓ cardiac output +

INHALED NO (FIRST LINE)	IV EPOPROSTENOL	IV ADENOSINE
10 to 20 ppm	2 - 12 ng/kg/min	50 to 350 µg/kg/min

- **Hepatic venous pressure gradient** = Wedged hepatic venous pressure - IVC pressure; normal value between 1-5 mmHg (≥ 10 mmHg → portal hypertension / cirrhosis)

MONITORING OF FUNCTIONAL CAPACITY: WHO functional class (equivalent to NYHA); 6MWT; Stress test; Cardiopulmonary test / VO₂ max

MANAGEMENT



O₂ (target: SaO₂ > 90% and PaO₂ > 60 mmHg)

AVOID PREGNANCY

REHABILITATION / AEROBIC EXERCISE PROGRAM

AVOID HIGH ALTITUDE; O₂ in plane when SaO₂ < 92% (or PaO₂ < 60 mmHg)

VACCINATION (Influenza - Pneumococcus)

SODIUM RESTRICTION (< 2.4 g/day) in the presence of volume overload

DIURETICS for volume overload

DIGOXIN (right heart failure or atrial tachyarrhythmias)

DRUG THERAPY FOR GROUP 1 PAH		
Anticoagulation	Warfarin Target INR: 2.0 to 2.5	Consider in idiopathic PAH or Heritable PAH or PAH due to anorexigens (class IIb recommendation)
Calcium channel blocking agents	Nifedipine (120 - 240 mg) Diltiazem (720 - 960 mg) Amlodipine (20 - 30 mg PO)	In patients with idiopathic PAH, Heritable PAH or drug induced PAH and positive vasoreactivity test Continue if WHO functional class 1 to 2/4 with marked hemodynamic improvement
Prostanoids (prostacyclins) Vasodilators Antiproliferative agents	Epoprostenol 2 ng/kg/min IV (target 25 - 40 ng/kg/min)	Only agent demonstrated to ↓ mortality in IPAH (★ Primary Pulmonary Hypertension Study Group) Need for intravenous administration (risk of local infection and catheter obstruction / sepsis)
	Treprostinil (SC or IV or inhaled) • s/c: 1-2 to 20 - 80 ng/kg/min • Inhaled: 30 - 45 µg qid	Associated with infusion site pain
	Iloprost aerosol 2.5 - 5 µg (6-9 per day)	Associated with flushing and jaw pain
Prostacyclin IP receptor agonist	Selexipag 200-1600 µg PO bid	Headache; Diarrhea; Nausea; Flushing
Endothelin receptor antagonist Vasodilator	Ambrisentan 2.5 - 5 - 10 mg PO qd	Adverse effects: liver function test abnormalities; edema
	Bosentan 125 mg PO bid	Monitor liver function monthly
	Macitentan 3 or 10 mg PO qd	Can cause anemia
Phosphodiesterase-5 inhibitor ↗ NO	Sildenafil 20 mg PO tid	Associated with headache, flushing, epistaxis
	Tadalafil 2.5 - 10 - 20 - 40 mg PO qd	Do not combine with soluble guanylatecyclase stimulator
Soluble guanylate cyclase stimulator ↗ NO	Riociguat 2.5 mg PO tid	Approved for group 1 PAH (★ PATENT) and thromboembolic PHT (★ CHEST) Risk of syncope Do not combine with PDE-5 inhibitor

BALLOON ATRIAL SEPTOSTOMY FOR RA-RV DECOMPRESSION: creation of a R → L shunt;

↘ RV filling pressures; improvement of LV filling; ↗ cardiac output (**at the cost of hypoxemia**)

- **Indications:** Severe PAH with treatment-refractory right heart failure (including inotropes) or recurrent syncope or bridge to transplant

LUNG TRANSPLANT: Progressive treatment-refractory PAH; WHO functional class 3-4/4

- **5-year survival:** 52-75%; risk of bronchiolitis obliterans - rejection - opportunistic infections

GROUP 2 PHT: left heart disease causing **venous PHT with passive retrograde transmission of increased pressure**

- **Wedge > 15 mmHg; Diastolic pressure gradient < 7 mmHg (dPAP - Mean Wedge)** **+**
- May be associated with pulmonary hemosiderosis (leakage of RBC from capillaries) with formation of fibrosis
- **Pulmonary artery vasodilators:** **risk of pulmonary edema in the presence of ↗ LV filling pressures** **+**
 - **PAH-approved therapies are not recommended in group 2 PHT**
 - **PDE-5 inhibitors / Macitentan:** awaiting the results of the ★ Sii-HF and ★ MELODY-1
- **Postcapillary PHT with precapillary component:** development of arterial PHT with ↗ PVR as mechanism of adaptation to pulmonary edema
 - **Active component:** ↗ pulmonary artery vasomotor tone and/or fixed obstructive arterial structural remodeling
 - **Diastolic pressure gradient ≥ 7 mmHg (dPAP - Mean Wedge)** **+**
 - **Consider pulmonary artery vasodilators** on an individual basis by the expert PH centre

GROUP 4 PHT: organized thrombus associated with the arterial wall with lobar or segmental or subsegmental perfusion abnormality

- Pulmonary arteriopathy superimposed (similar to idiopathic PAH)
- **V/Q scan:** screening test of choice
 - CT pulmonary angiography / Conventional pulmonary angiography for confirmation
- **Thromboendarterectomy:** treatment of choice (deep hypothermia circulatory arrest)
 - Consider balloon pulmonary angioplasty if technically non-operable
- **Anticoagulation** for life
- **Consider pulmonary artery vasodilators** when thromboendarterectomy is impossible or gives mixed results; prefer Riociguat (beneficial in ★ CHEST)

PAH ASSOCIATED WITH CONGENITAL HEART DISEASE (SHUNT)

EISENMENGER	PAH WITH L→R SHUNT	PAH WITH SMALL SEPTAL DEFECT	POST-CORRECTION PAH
<ul style="list-style-type: none"> • Large defect • Severely ↗ PRV • Reversed shunt (or bidirectional) • Cyanosis; Erythrocytosis; multisystem features 	<ul style="list-style-type: none"> • Moderate-to-large defect • No cyanosis at rest • Do not operate if PVR > 4.6 WU (or indexed PVR > 8 WU/m²) 	<ul style="list-style-type: none"> • VSD < 1 cm • ASD < 2 cm • ↗ PVR disproportionate to congenital anomaly • Similar profile to idiopathic PAH 	<ul style="list-style-type: none"> • PAH despite absence of a residual defect

- **Shunt distal to the tricuspid valve** (VSD; patent ductus arteriosus; truncus arteriosus) subjects pulmonary arteries to much higher pressure stress than pre-tricuspid shunt

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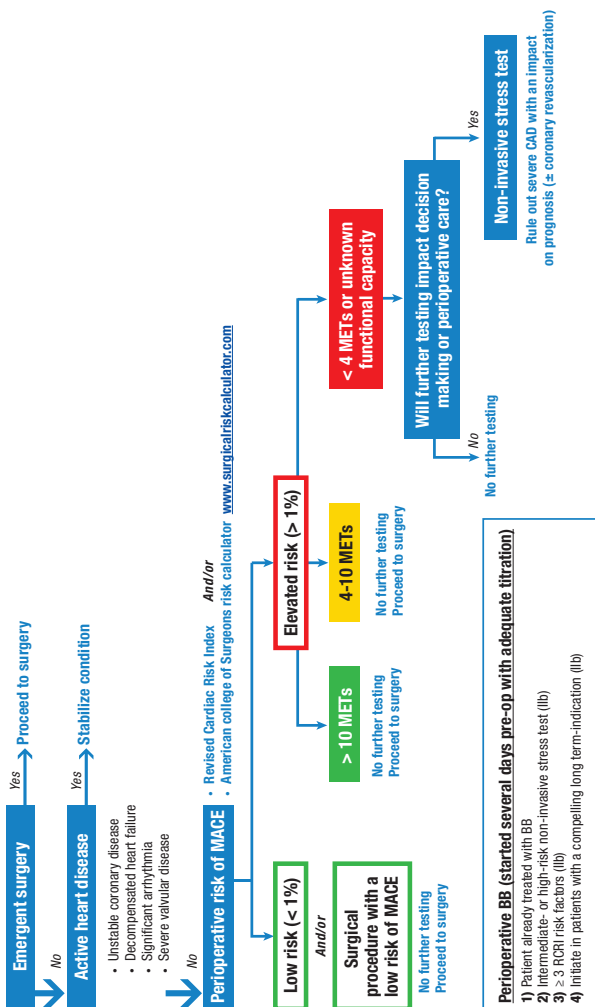
Miscellaneous

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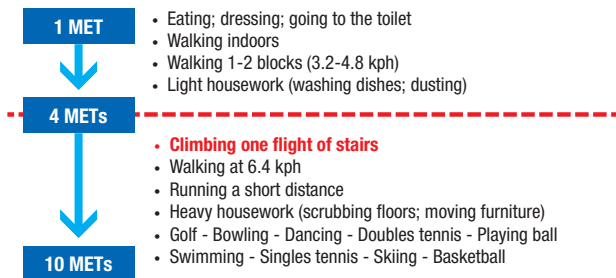
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9.1/ PREOPERATIVE ASSESSMENT (noncardiac surgery)

PREOPERATIVE ASSESSMENT - NON-CARDIAC SURGERY



EVALUATION OF FUNCTIONAL CAPACITY



09

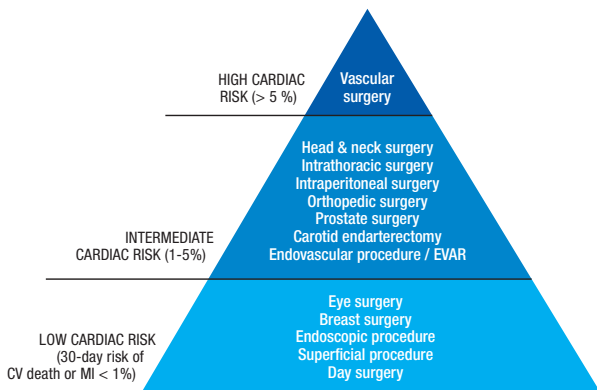
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REVISED CARDIAC RISK INDEX (RCRI) DURING NONCARDIAC SURGERY

<ol style="list-style-type: none"> 1) History of CAD 2) History of heart failure 3) History of cerebrovascular disease 4) Insulin-treated DM 5) Pre-op Creatinine > 2 mg/dL (> 176 mmol/L) 6) Intrathoracic or intraperitoneal or vascular surgery 	<p>Risk of cardiac events (MI; pulmonary edema; VF; cardiac arrest; complete heart block)</p> <p>0 point = low risk (0.5%) 1 point = moderate risk (1.3%) 2 points = moderate risk (3.6%) ≥ 3 points = high risk (9.1%)</p>
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CARDIAC RISK ASSOCIATED WITH SURGERY



NONINVASIVE STRATIFICATION

OBJECTIVE: to exclude the presence of severe CAD with an impact on prognosis and which would require revascularization, regardless of the type of surgery

PREOPERATIVE REVASCULARIZATION: no benefit on perioperative events, even in the presence of significant ischemia on noninvasive stratification (★ CARP; ★ DECREASE-V)

INDICATIONS FOR PREOPERATIVE REVASCULARIZATION: identical to stable CAD or unstable angina or NSTEMI or STEMI (▶▶| Chapter 2 - CAD) +

PERIOPERATIVE BETA-BLOCKERS AND STATINS

BB - INDICATIONS: 1) Patient already treated with BB (Class I recommendation); 2) Intermediate- or high-risk non-invasive stress test (IIb); 3) ≥ 3 RCRI risk factors (IIb); 4) Initiate in patients with a compelling long term indication (IIb)

BB - MODALITIES OF USE: Start BB therapy several days preoperatively; titrate the dose targeting a resting HR of 60-80 bpm; avoid hypotension

- ★ **POISE:** High-dose Metoprolol succinate started 2-4 h preoperatively versus placebo;
 - ↳ primary outcomes (cardiovascular mortality; MI) but ↗ all-cause mortality and ↗ stroke

STATINS - INDICATIONS: 1) Patient already on statin (I); 2) Initiate if undergoing vascular surgery (IIa); 3) Initiate in patients with clinical indications who are undergoing elevated-risk procedures (IIb)

PERIOPERATIVE ECG AND TROPONIN

ECG: Preoperative → CAD, arrhythmia, PAD, cerebrovascular disease or structural heart disease (except for low-risk procedures); **Post-operative** → **A)** Signs or symptoms suggestive of ischemia / MI / arrhythmia; **B)** Usefulness of routine screening in asymptomatic patient is uncertain (IIb)

POSTOPERATIVE TROPONIN: Indications → **A)** Signs or symptoms suggestive of ischemia or MI; **B)** Usefulness of routine screening in asymptomatic patient is uncertain (IIb)

DIAGNOSIS OF PERIOPERATIVE MYOCARDIAL INFARCTION: ▶▶| Chapter 2 (Definition of MI)

- Consider type 1 myocardial infarction (rupture of fragile plaque) or type 2 (O₂ supply/demand mismatch); Type 1 MI causes < 5% of troponin elevation postoperatively +

PERMANENT PACEMAKER AND DEFIBRILLATOR

PACEMAKER-DEPENDENT PATIENT: Reprogram in V00 or D00 mode or apply a magnet during the operation (asynchronous stimulation)

DEFIBRILLATOR: Temporarily deactivate tachyarrhythmia therapies or apply a magnet during the operation

- **N.B.:** a magnet applied to a defibrillator deactivates tachyarrhythmia therapies, but does not change the pacing mode to V00 or D00; risk of inappropriate inhibition of pacing

SPECIFIC ENTITIES

HCM: avoid dehydration / vasodilators / hypotension / beta-agonists

SEVERE AORTIC STENOSIS

- **Asymptomatic:** complete preoperative clinical reassessment with stress test; consider AVR before elective high-risk non-cardiac surgery; monitor intravascular volume; avoid tachycardia; avoid intraoperative hypotension (treat with phenylephrine)
- **Patient refusing AVR or not a candidate or requiring urgent surgery:** operative mortality $\geq 10\%$; consider TAVI or balloon valvuloplasty if hemodynamically unstable

POST-PCI SURGERY AND DUAL ANTIPLATELET THERAPY

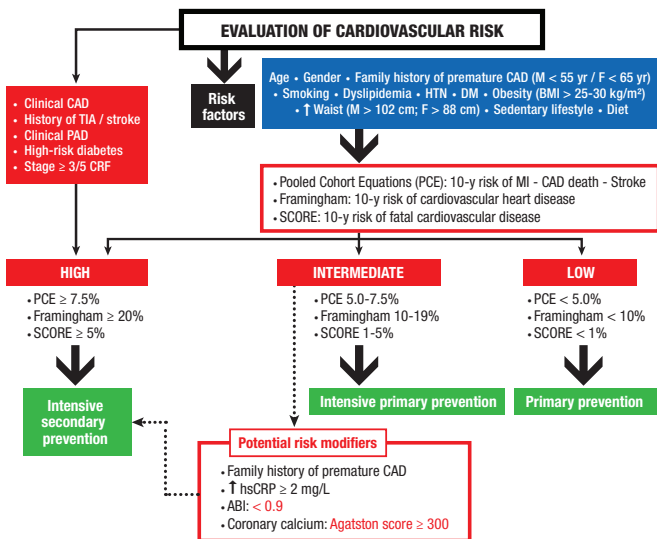
- **Post-PTCA:** wait **2-4 weeks** (then operate under ASA)
- **Post-BMS:** dual antiplatelet therapy for a minimum of **2-4 weeks** (then operate under ASA)
 - Discontinue Clopidogrel 5-7 days preoperatively
- **Post-DES:** dual antiplatelet therapy for a **strict minimum of 3 to 6 months** with new generation stents (consider bridging with IV tirofiban / eptifibatide / cangrelor if surgery required before this time) then operate under ASA

	MECHANICAL VALVE PROSTHESIS	ATRIAL FIBRILLATION	THROMBOEMBOLIC DISEASE
High thromboembolic risk (annual risk > 10%)	<ul style="list-style-type: none"> • Mitral valve prosthesis • Old generation aortic valve prosthesis (cagedball; tilting-disk) • Stroke or TIA < 6 months 	<ul style="list-style-type: none"> • CHADS 5 or 6 • Stroke or TIA < 3 months • Rheumatic disease 	<ul style="list-style-type: none"> • Thromboembolism < 3 months • Severe thrombophilia (protein C or S or antithrombin deficiency; antiphospholipid antibodies; multiple anomalies)
	<ul style="list-style-type: none"> • Stop Warfarin 5 days pre-op + Bridge with IV heparin or LMWH • Prosthetic Valve or AF → Enoxaparin 1 mg/kg bid or Dalteparin 100 IU/kg bid; Venous thromboembolism → Enoxaparin 1.5 mg/kg qd or Dalteparin 200 IU/kg qd • INR on the day before surgery (vitamin K 1 mg PO if INR > 1.5) • Stop IV Heparin 4-6 h pre-op; Last dose of LMWH 24 h pre-op (Enoxaparin 1 mg/kg or Dalteparin 100 IU/kg administered 24 h pre-op) • Resume Warfarin 12-24 h post-op if adequate hemostasis • Resume Heparin (without bolus) or LMWH 48-72 h post-op depending on hemostasis • Consider IVC filter in the presence of venous thromboembolism < 4 weeks 		
Moderate thromboembolic risk (annual risk 5-10%)	<u>Bileaflet aortic valve prosthesis with ≥ 1 risk factor:</u> AF • History of stroke or TIA • HTN • DM • Heart failure • > 75 years	CHADS 3 or 4 (no benefit in ★BRIDGE; mean CHADS = 2.3)	<ul style="list-style-type: none"> • Thromboembolism 3-12 months • Nonsevere thrombophilia: Leiden factor V or prothrombin mutation (heterozygous) • Active neoplasia
	<ul style="list-style-type: none"> • Case-by-case decision for heparin bridge (thromboembolic risk versus perioperative bleeding risk) 		
Low thromboembolic risk (annual risk < 5%)	Bileaflet aortic valve prosthesis with no other risk factor	CHADS 0 to 2 (with no history of stroke or TIA)	Thromboembolism > 12 months (with no other risk factor)
	<ul style="list-style-type: none"> • Heparin bridge not recommended 		

MINOR PROCEDURES: do not discontinue Warfarin for superficial skin or ophthalmic (cataract) or dental procedures (use tranexamic acid)

9.2/ PRIMARY & SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

EVALUATION OF THE RISK OF ADVERSE CARDIOVASCULAR EVENTS



CARDIOVASCULAR DISEASE - PRIMARY PREVENTION

CONTROL OF CONVENTIONAL RISK FACTORS: ►► Smoking cessation; ►► Dyslipidemia; ►► HTN; ►► DM; ►► Weight & Diet; ►► Physical exercise

ASA: not recommended as part of routine primary prevention

- ★ **Antithrombotic Trialists' Collaboration:** marginal benefit of ASA for primary prevention (high NNT); bleeding risk
- **Consider ASA for primary prevention:** in the presence of a low bleeding risk but high cardiovascular risk (subclinical atherosclerosis; multiple risk factors; family history of premature cardiovascular disease) (Class IIb recommendation; C)

CARDIOVASCULAR DISEASE - SECONDARY PREVENTION

Smoking	Complete cessation
Dyslipidemia	High dose statin; Target → ≥ 50% ↓ LDL
HTN	Target BP < 140/90 (< 140/85 in the presence of DM)

Antiplatelet therapy	ASA: for life (★ Antithrombotic Trialists*) • Clopidogrel as alternative (★ CAPRIE) • No benefit of ASA + Clopidogrel combination (★ CHARISMA)
ACE inhibitors	As secondary prevention for all patients (especially when LVEF \leq 40% or HTN or DM or CRF)
BB	• LVEF \leq 40%: Long term • Normal LVEF: can be stop 3 years after ACS • Antianginal: Long term
DM	HbA1c $<$ 7%
Physical exercise	$>$ 30 min moderate exercise 5 x per week
Obesity	• BMI: 18.5 - 24.9 kg/m ² • Waist: M $<$ 102 cm and F $<$ 88 cm
Healthy diet	Healthy and balanced diet
Influenza vaccine	Annually
Hormonal therapy; NSAID	Avoid

9.3/ SMOKING CESSATION

30% of deaths related to CAD can be attributed to smoking

BENEFITS: reduction of cardiovascular risk to achieve a similar level to that of nonsmokers after 5 years of smoking cessation

INTERVENTION

1) Confirm that the patient is a smoker; **2)** Strongly recommend smoking cessation; **3)** Ask the patient whether he/she wants to stop smoking (if the patient refuses, suggest reducing consumption \pm nicotine replacement therapy); **4)** Establish a plan and a date for complete cessation; **5)** Inform the patient's friends and relatives; **6)** Remove all objects related to smoking; **7)** Cease all activities related to smoking; **8)** Have a plan in the case of temptation / relapse; **9)** Propose drug therapy; **10)** Propose support by a smoking cessation center; **11)** www.smokefree.gov; **12)** Ensure regular follow-up

DRUG THERAPY

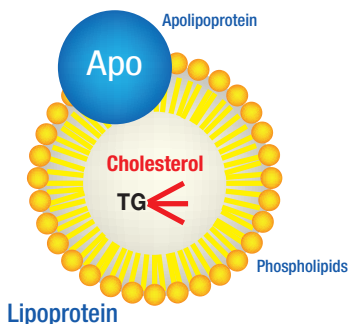
Nicotine gum	Initially 1 gum every 1–2 h then decrease (maximum: 24 gums per day) • \leq 24 cigarettes / day: 2 mg gum • \geq 25 cigarettes / day: 4 mg gum	• 6-month abstinence rate: 19% • Adverse effects: Nausea; Oropharyngeal irritation
Transdermal nicotine patch	• $<$ 10 cigarettes / day: 14 mg patch for 6 weeks then 7 mg patch for 4 weeks then stop • $>$ 10 cigarettes / day: 21 mg patch for 6 weeks then 14 mg patch for 2 weeks then 7 mg patch for 2 weeks	• 6-month abstinence rate: 23% • Adverse effects: Local skin reaction; Nausea; Insomnia
Bupropion SR	• Inhibits dopamine and norepinephrine reuptake • Bupropion SR 150 mg PO daily for 3 days then bid for 12 weeks then stop • Start 10 days before smoking cessation • Can be combined with nicotine replacement therapy	• 6-month abstinence rate: 24% • Adverse effects: Decreased seizure threshold; Insomnia; Xerostomia; Nightmares

Varenicline	<ul style="list-style-type: none"> • Partial agonist of acetylcholine nicotinic receptor • Varenicline 0.5 mg PO daily for 3 days then bid for 3 days then 1 mg bid for 11 weeks then stop • Start 1 to 2 weeks before smoking cessation • Can be combined with nicotine replacement therapy 	Contraindicated in the case of pregnancy or breastfeeding or CRF or mental illness
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9.4/ DYSLIPIDEMIA

DIET: source of triglycerides (glycerol bound to 3 fatty acid chains) and dietary Cholesterol

LIPOPROTEINS: transport TG and cholesterol in the blood



CHYLOMICRONS: large nonatherogenic lipoproteins transporting TG from the gastrointestinal tract; apoB48

VLDL: large nonatherogenic lipoproteins transporting TG from the liver; apoB100

LDL: atherogenic lipoproteins responsible for atherosclerosis; mainly contain cholesterol; apoB100

+

> **Calculated LDL (mmol/L) = TC - HDL - (0.45 x TG) (valid if TG < 4.5 mmol/L)**

> **Calculated LDL (mg/dL) = TC - HDL - (TG / 5) (valid if TG < 400 mg/dL)**

NON-HDL CHOLESTEROL (= TC - HDL): cholesterol contained in LDL - VLDL - IDL - Lp(a); predictive of cardiovascular risk

> **ApoB:** comprises LDL - VLDL - IDL - Lp(a)

HDL: antiatherogenic properties; contains apolipoprotein ApoA1

HYPERTRIGLYCERIDEMIA: TG-enriched LDL → formation of smaller and denser LDL (due to modification by hepatic lipase) → dense, atherogenic LDL

+

> **HyperTG:** TG-enriched HDL (CTEP) → ↗ recovery of HDL by the liver → ↘ HDL

+

> **HyperTG:** associated with metabolic syndrome (↗ TG; ↘ HDL; dense, atherogenic LDL)

+

> **HyperTG:** risk of pancreatitis (especially if TG > 10 mmol/L or > 885 mg/dL)

LP(a): apolipoprotein(a) bound to a molecule of LDL; associated with an increased risk of cardiovascular events; plasma concentration is genetically determined

SCREENING FOR DYSLIPIDEMIA

- Male ≥ 40 years
- Female ≥ 50 years (or postmenopausal)
- DM
- HTN
- Smoking
- BMI > 27 kg/m²
- CRF - CrCl < 60 mL/min
- Atherosclerosis
- Family history of premature CAD (M < 55 years; F < 65 years)
- Family history of dyslipidemia
- SLE - RA - Psoriatic arthritis - Ankylosing spondylitis - Inflammatory bowel disease
- COPD
- Erectile dysfunction
- HIV (treated with antiretroviral agents)
- Clinical features of familial dyslipidemia (xanthomas; xanthelasmas; arcus senilis)

DYSLIPIDEMIA: UNDERLYING CAUSES

HYPERCHOLESTEROLEMIA: Hypothyroidism; Cholestasis; Nephrotic syndrome; CRF; Cushing; Corticosteroids; Anorexia; HIV protease inhibitors

HYPERTRIGLYCERIDEMIA: Obesity; DM; Alcohol; CRF; Hypothyroidism; Corticosteroids; Antipsychotics (Clozapine; Olanzapine); Nonselective BB; Thiazides; Cyclosporine; HIV protease inhibitors; Retinoic acid; Hormonal therapy; Sirolimus; Bile acid sequestrants

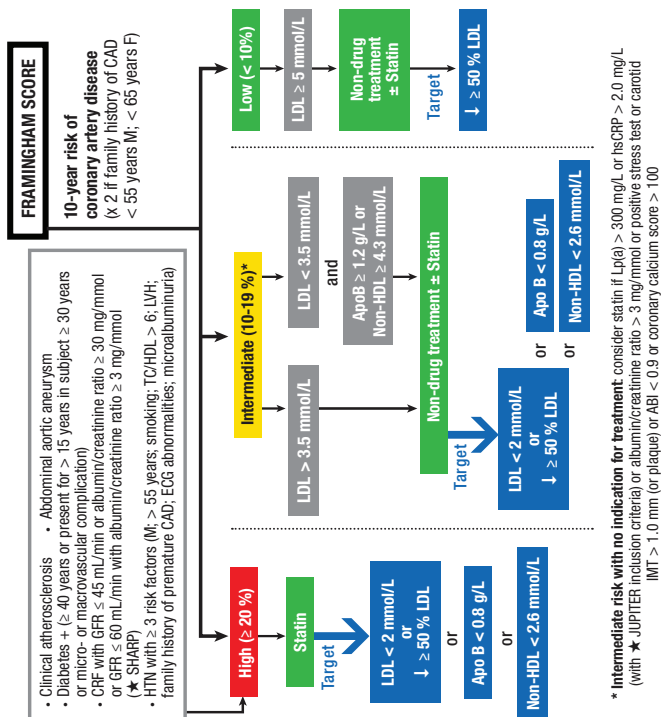
↘ **HDL:** Smoking; Obesity; Sedentary lifestyle; DM; CRF; HyperTG; Nonselective BB; Corticosteroids; Anabolic steroids; Cyclosporine

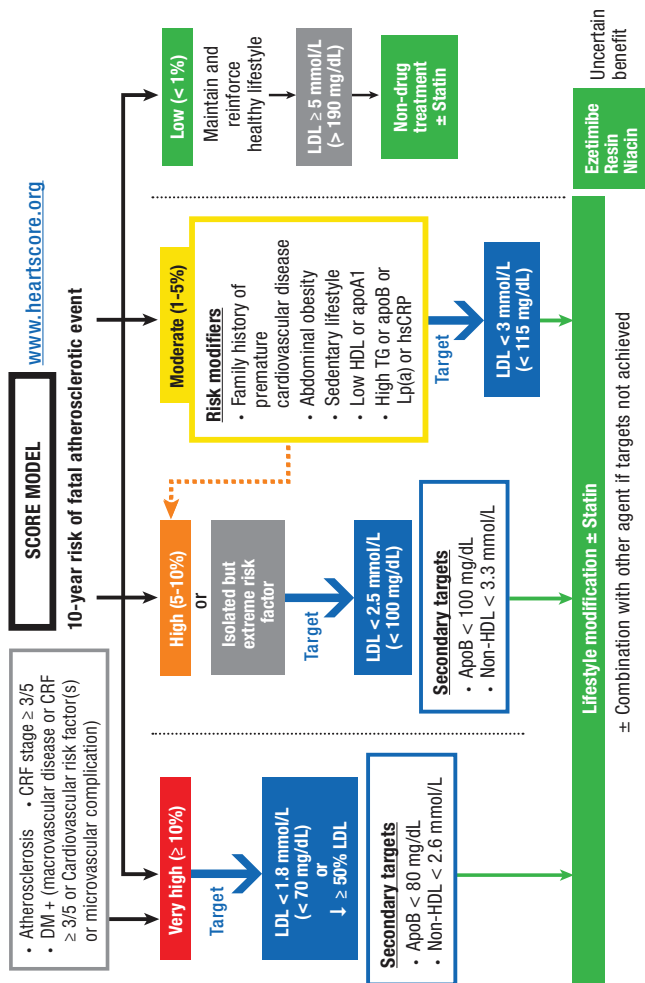
GENETIC DISORDERS OF LIPOPROTEINS

Familial hypercholesterolemia	↗ LDL	<ul style="list-style-type: none"> • LDL-R receptor mutation • 1,000 mutations identified • Autosomal dominant 	<ul style="list-style-type: none"> • Arcus senilis • Xanthelasmas • Pathognomonic tendinous xanthomas (extensor tendons; MCP; Achilles tendon) • Premature CAD
Defective Apo B100	↗ LDL	<ul style="list-style-type: none"> • ↘ Affinity for LDL-R receptor • Autosomal dominant 	<ul style="list-style-type: none"> • Similar presentation to familial hypercholesterolemia
Familial LPL deficiency	↗ TG	<ul style="list-style-type: none"> • Abnormal catabolism of chylomicrons and VLDL 	<ul style="list-style-type: none"> • Pancreatitis • Lipemia retinalis • Eruptive xanthomas • Lactescent serum
Familial Apo-C-II deficiency	↗ TG	<ul style="list-style-type: none"> • Apo-CII is the LPL activator 	<ul style="list-style-type: none"> • Similar presentation to familial LPL deficiency
Familial dysbeta-lipoproteinemia	↗ TC ↗ TG	<ul style="list-style-type: none"> • Homozygote for ApoE2 (less effective binding to hepatic receptors) • Accumulation of remnant lipoproteins (IDL; remnant chylomicrons) 	<ul style="list-style-type: none"> • Premature CAD • Tuberous xanthomas (elbows; knees) • Palmar xanthomas • Consider diagnosis: ApoB (g/L) / TC (mmol/L) ratio < 0.15

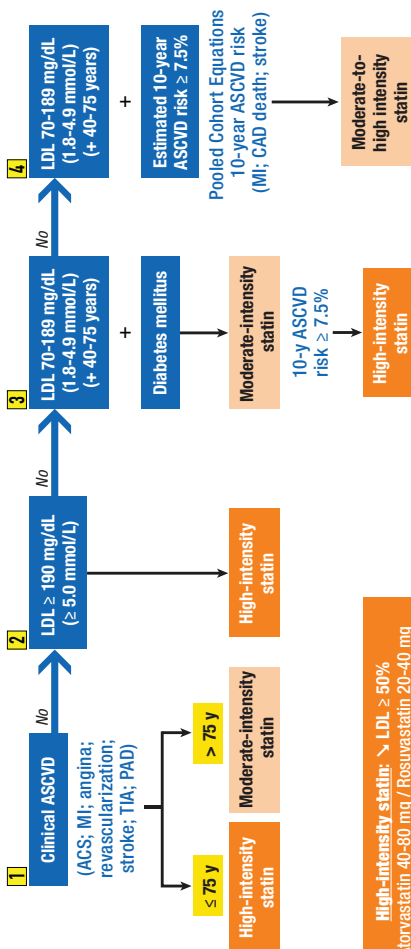
Familial combined hyperlipidemia	A) \nearrow VLDL (\nearrow TG) or B) \nearrow LDL (\nearrow TC) or C) \nearrow VLDL and \nearrow LDL (\nearrow TG and \nearrow CT)	<ul style="list-style-type: none"> 1-2% of the population Extremely heterogeneous Interactions between multiple genes and environment Hepatic overproduction of lipoproteins apo-B100 (associated with VLDL) Defective LPL in 1/3 of patients (\nearrow TG) 	<ul style="list-style-type: none"> Xanthelasma Arcus senilis Premature CAD Dense, atherogenic LDL Consider diagnosis: Apo B > 120 mg/dL + TG > 1.5 mmol/L + family history of premature CAD
	Familial \searrow HDL	\searrow HDL	a) Apo A-I deficiency b) Tangier (CERP protein dysfunction) c) Familial LCAT deficiency

MANAGEMENT - CANADIAN TARGETS





MANAGEMENT - AMERICAN TARGETS



High-intensity statin: > LDL ≥ 50%
Atorvastatin 40-80 mg / Rosuvastatin 20-40 mg

Moderate-intensity statin: > LDL 30-50%
Atorvastatin 10-20 mg / Rosuvastatin 5-10 mg /
Simvastatin 20-40 mg / Pravastatin 40-80 mg

Less evidence for statin therapy
in NYHA II-IV HF or Hemodialysis

ASCVD: Atherosclerotic cardiovascular disease

Consider statin therapy

- LDL ≥ 160 mg/dL (≥ 4.1 mmol/L)
- Evidence of genetic hyperlipidemia
- Family history of premature ASCVD (< 55 y M - < 65 y F)
- Hs-CRP ≥ 2 mg/L
- CAC ≥ 300 Agatston units
- ABI < 0.9

NONDRUG TREATMENT: healthy diet; diet rich in omega-3 fatty acids; target healthy weight (BMI 18.5 to 24.9 kg/m²); regular physical exercise; smoking cessation; moderate alcohol consumption (maximum: 2 glasses per day for M and 1 glass per day for F)

DRUG TREATMENT: First-line Statin

HYPERTRIGLYCERIDEMIA: avoid alcohol and secondary causes; ↓ carbohydrates; increase omega-3 consumption; exercise and weight loss; control of DM

- **TG > 10 mmol/L (> 885 mg/dL) → Fibrate for prevention of pancreatitis**
- **TG 5-10 mmol/L (440-885 mg/dL) → Consider Fibrate (undemonstrated benefit)**

↘ **HDL:** smoking cessation; weight loss; exercise; moderate alcohol consumption

- **Niacin:** no benefit in ★ AIM-HIGH and ★ HPS2-THRIVE studies

STATINS (HMG-COA REDUCTASE INHIBITORS)		
Atorvastatin	10-80 mg	<ul style="list-style-type: none">• ↘ LDL (30-50%)• ↘ TG (10-30 %); ↗ HDL (5-10 %)• ↘ intracellular cholesterol synthesis → ↗ expression of LDL-R receptor• Pleiotropic effects: stabilization of atherosclerotic plaque; antiinflammatory effect; antithrombotic effect; improves endothelial function• Adverse effects: ↗ Transaminases; Myalgia / Myositis / Rhabdomyolysis; Drug interactions; ↗ risk of DM
Fluvastatin	20-80 mg	
Lovastatin	20-80 mg	
Pravastatin	10-40 mg	
Rosuvastatin	5-40 mg	
Simvastatin	10-40 mg	
BILE ACID SEQUESTRANTS (RESINS)		
Colesevelam	4 to 6 tablets (in 1 or 2 daily doses)	<ul style="list-style-type: none">• ↘ LDL (15-30 %)• Adverse effects: GI symptoms (constipation; discomfort); ↘ absorption of medications; ↗ TG
Colestipol	1 or 5 g / unit; 2-6 units / days (with meals)	
CHOLESTEROL ABSORPTION INHIBITOR		
Ezetimibe	10 mg	<ul style="list-style-type: none">• ↘ LDL (20 %)• Interferes with NPC1-L1 protein of intestinal epithelial cells• ★ IMPROVE-IT: Ezetimibe + Simvastatin vs. Simvastatin post ACS; ↘ MI and Stroke
FIBRATES		
Fenofibrate	200 mg	<ul style="list-style-type: none">• ↘ TG (35-50 %)• ↗ HDL (5-10 %); ↘ LDL (10-20 %)• ↗ LPL activity; ↘ Hepatic secretion of VLDL• No benefit in ★ ACCORD study• Adverse effects: ↗ Creatinine (adjust according to CrCl); Myotoxicity (avoid Gemfibrozil with statin); Rash; Drug interactions; ↗ Transaminases
Bezafibrate	400 mg	
Gemfibrozil	600 mg bid	

NICOTINIC ACID		
Niacin	1 g tid	<ul style="list-style-type: none"> • ↗ HDL (25 %); ↘ TG (30 %); ↘ LDL (20 %) • ↗ Hepatic production of apo A1 • ↘ HDL catabolism • ↘ Hepatic production of VLDL • No benefit in ★ AIM-HIGH and ★ HPS2-THRIVE studies • Adverse effects: Flushing (↘ with ASA); Hyperuricemia; Hyperglycemia; Hepatotoxicity; Gastritis
Slow-release niacin (Niaspan)	1-2 g daily	
CETP INHIBITORS		
↗ HDL; Anacetrapib; Dalcetrapib (no benefit in ★ dal-OUTCOMES); Evacetrapib		
PCSK9 INHIBITORS		
↘ LDL ★ ODYSSEY long term: ↘ LDL (62 %); ↘ MACE with Alirocumab vs. Placebo ★ OSLER: ↘ LDL (61 %); ↘ cardiovascular events and MACE with Evolocumab vs. Placebo		

STATINS

★ **CHOLESTEROL TREATMENT TRIALISTS':** each 1 mmol/L (40 mg/dL) ↘ of LDL → 20-25% ↘ RR of cardiovascular mortality or myocardial infarction +

PRIMARY PREVENTION: ★ WOSCOPS (Pravastatin); ★ AFCAPS/TexCAPS (Lovastatin); ★ HPS (Simvastatin); ★ ASCOT (Atorvastatin); ★ JUPITER (Rosuvastatin)

SECONDARY PREVENTION: ★ 4S (Simvastatin); ★ CARE (Pravastatin); ★ LIPID (Pravastatin); ★ HPS (Simvastatin)

▷ **Intensive treatment:** ★ A-to-Z and ★ SEARCH (Simvastatin); ★ PROVE-IT, ★ TNT, ★ ALLIANCE, ★ IDEAL and ★ SPARCL (Atorvastatin)

ADVANCED HEART FAILURE (LVEF < 30 %): no benefit (★ CORONA; ★ GISSI-HF)

RENAL FAILURE ON DIALYSIS: no benefit (★ 4D; ★ AURORA)

MONITORING OF STATIN THERAPY

LIPID PROFILE: At 4 to 12 weeks; then annually when dose adjusted and targets achieved

DECREASING DOSE: may be considered when LDL < 1.0 mmol/L (< 40 mg/dL) +

MYALGIA: Discontinue Statin then resume several weeks later to **prove toxicity** (+ monitoring of CK)

▷ **Proven toxicity:** **A)** Reintroduce the same statin at a lower dose; **B)** Fluvastatin; **C)** Rosuvastatin 5-10 mg daily (or every 2 days or once a week); **D)** Ezetimibe - Niacin - Fibrate

▷ **Consider other conditions:** Hypothyroidism; CRF; liver disease; PMR; steroid myopathy; vitamin D deficiency; primary muscle diseases

MYOSITIS: myalgia + ↗ CK > ULN

RHABDOMYOLYSIS: severe myalgia; CK > 10,000 IU/L; Myoglobinuria; ± ARF

RISK FACTORS FOR MYOPATHY: statin dose; drug interactions; > 75 years; CRF (prefer Atorvastatin); liver disease; alcohol; pre-existing myopathy

AST – ALT		CK	
Baseline measurement and as necessary		Assay as necessary in the presence of myalgia	
$\nearrow < 3 \times \text{ULN}$	$\nearrow \geq 3 \times \text{ULN}$	$\nearrow \leq 5 \times \text{ULN}$	$\nearrow > 5 \times \text{ULN}$
<ul style="list-style-type: none"> Continue treatment AST - ALT in 6 weeks If stable \rightarrow stop monitoring AST - ALT 	<ul style="list-style-type: none"> Discontinue Statin Consider DDx (alcohol; drugs; NASH) Monitor AST - ALT until normalization <p>Normalization</p> <ol style="list-style-type: none"> Reintroduce at a lower dose Different statin Ezetimibe - Niacin - Fibrate 	<ul style="list-style-type: none"> Continue statin in the absence of symptoms Repeat CK in 6 weeks Discontinue Statin in the presence of symptoms or \nearrow CK If stable and asymptomatic \rightarrow stop monitoring CK 	<ul style="list-style-type: none"> Discontinue Statin Consider rhabdomyolysis (\pm hydration) Monitor CK until normalization Consider DDx <p>Normalization</p> <ol style="list-style-type: none"> Reintroduce at a lower dose Different statin Ezetimibe - Niacin - Fibrate

9.5/ HYPERTENSION

ASSESSMENT

DIAGNOSIS OF HYPERTENSION		
Office	1st VISIT: SBP ≥ 140 and/or DBP ≥ 90	
	SUBSEQUENT VISIT: <ul style="list-style-type: none"> Diagnosis of HTN if target organ damage or DM or GFR < 60 mL/min Diagnosis of HTN if SBP ≥ 180 and/or DBP ≥ 110 Otherwise <ul style="list-style-type: none"> Office: diagnosis of HTN if SBP ≥ 160 and/or DBP ≥ 100 x first 3 visits (mean) Office: diagnosis of HTN if SBP ≥ 140 and/or DBP ≥ 90 x first 5 visits (mean) ABPM or BP measured at home 	
ABPM (24 h)	<ul style="list-style-type: none"> Daytime SBP: ≥ 135 or 24-hour SBP: ≥ 130 or Night: SBP ≥ 120; $\searrow < 10\%$ 	<ul style="list-style-type: none"> Daytime DBP: ≥ 85 or 24-hour DBP: ≥ 80 or Night: DBP ≥ 70; $\searrow < 10\%$
BP at home	Daytime SBP: ≥ 135 mmHg	Daytime DBP: ≥ 85 mmHg
	<ul style="list-style-type: none"> ≥ 2 readings daily (on getting out of bed and at bedtime) for 7 days (mean of days 2 to 7) Recommended apparatus: www.hypertension.ca 	
Hypertensive emergency	HTN diagnosed immediately	

STAGE OF HTN		
Grade 1 140-159 and/or 90-99	Grade 2 160-179 and/or 100-109	Grade 3 ≥ 180 and/or ≥ 110

BLOOD PRESSURE MEASUREMENT TECHNIQUE

a) After resting for 5 min; no coffee or cigarettes for > 30 min; legs uncrossed; **b)** Patient seated in a chair with a back with the arms level with the heart; **c)** Inflatable cuff covers > 80% of the arm circumference; Cuff > 3 cm above the cubital fossa; **d)** Inflate to 30 mmHg above the level at which the radial pulse is lost; **e)** Deflate by 2 mmHg per beat; **f)** ≥ 3 measurements on the same arm (determine the mean of the last 2 measurements); **g)** Measure BP in both arms; **h)** Measure BP 1 min and 3 min after standing (rule out OH)

- **First audible sound = SBP (Korotkoff phase I)**
- **Last audible sound = DBP (Korotkoff phase V)**
 - If sounds persist until 0 mmHg, use the point at which the sounds become softer to define DBP (phase IV)

WORK-UP: Electrolytes; Creat; Urinalysis; Albumin/creat ratio; Fasting glucose; Lipids; CBC; ECG

ABPM (AMBULANT BLOOD PRESSURE MONITORING): verify response to treatment; nocturnal HTN (insomnia; OSAHS; obesity; CRF; OH; dysautonomia); evaluate fluctuating BP

- **White coat syndrome:** high BP in the doctor's office; home BP or daytime ABPM < 130-135/80-85 mmHg; no signs of target organ damage
- **Masked HTN:** normal BP in the doctor's office; ↗ daytime BP (stress; work...)

SEARCH FOR TARGET ORGAN DAMAGE

HEART DISEASE: CAD; Heart failure; LVH (ECG; TTE)

CEREBROVASCULAR DISEASE: stroke; TIA; Intracerebral hemorrhage; SAH; Vascular dementia; Carotid IMT ≥ 1 mm or plaques

PERIPHERAL ARTERY DISEASE (PAD): Aortic dissection; AAA; Claudication - Leg ischemia; ABI < 0.9

RENAL DISEASE: Hypertensive nephroangiosclerosis; CrCl < 60 mL/min; Microalbuminuria (30-300 mg/24 h or albumin/creatinine ratio 3.4-34 mg/mmol or 30-300 mg/g) or Macroalbuminuria

HYPERTENSIVE RETINOPATHY: Hemorrhages; microaneurysms; cotton wool spots or hard exudates; papilledema

UNDERLYING CAUSES OF HYPERTENSION

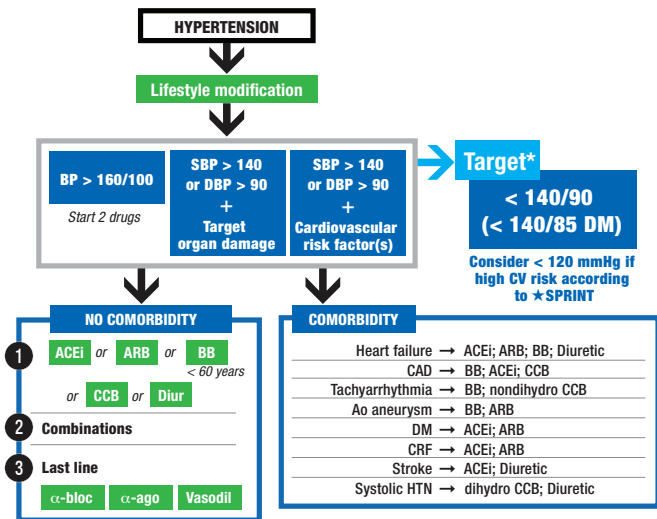
LOOK FOR AN UNDERLYING CAUSE IN THE PRESENCE OF: severe HTN; sudden onset or sudden deterioration of HTH; treatment failure; target organ damage disproportionate to the duration of HTN

Chronic renal disease	<ul style="list-style-type: none"> • Salt and water retention / Volume overload 	<ul style="list-style-type: none"> • Urinalysis; Creatinine; Renal US; ± biopsy
Renovascular disease	<ul style="list-style-type: none"> • ▶▶ Chapter 8 (Peripheral vascular disease) 	<ul style="list-style-type: none"> • Doppler renal arteries; MR angiography; CT angiography
CoA	<ul style="list-style-type: none"> • HTN in arms; ↘ Femoral pulses; Murmur between scapulae 	<ul style="list-style-type: none"> • TTE; MR angiography; CT angiography; Cardiac cath
Primary hyperaldosteronism	<ul style="list-style-type: none"> • Adenoma; Adrenal hyperplasia • Hypokalemia (spontaneous or severe diuretic-induced); Refractory HTN; ± Hypnatremia; Muscle weakness 	<ul style="list-style-type: none"> • ↗ Plasma Aldosterone / Renin ratio (high sensitivity) • Suppression test with salt load (absence of ↘ of Aldosterone) • Adrenal CT scan or MRI • Adrenal vein catheterization

Cushing syndrome	<ul style="list-style-type: none"> • Truncal obesity; Violaceous striae; Thin skin; Muscle wasting; Osteoporosis; Buffalo hump 	<ul style="list-style-type: none"> • Urinary cortisol • Suppression test (1 mg dexamethasone) • CT scan of adrenal glands
Pheochromocytoma	<ul style="list-style-type: none"> • Labile HTN; Headache; Profuse sweating; Palpitations • Exacerbated by stress / anesthesia / BB / caffeine / manipulation of the tumor • \pm Dilated CM with HTN • Associated with Von Hippel-Lindau syndrome; MEN; Neurofibromatosis 	<ul style="list-style-type: none"> • Plasma metanephrines (sensitivity 99%) • Urine metanephrines • CT scan or MRI of adrenal glands
Medications - Drugs	NSAID; Corticosteroids; Cyclosporine; Tacrolimus; EPO; Ephedrine; Decongestants; Cocaine; Amphetamines; Oral contraceptive; MAO inhibitors - SSRI; Midodrine; Anabolic steroids	

Other: Acromegaly; Hypothyroidism; Hyperparathyroidism; Pregnancy; Acute glomerulonephritis; Renal crisis (scleroderma); Rebound HTN (nonadherence to treatment); Smoking; Alcohol; Obesity; Sodium; OSAHS; Liquorice; Chronic pain; Intracranial neoplasm

MANAGEMENT



* AMERICAN TARGETS (JNC 8)

- < 60 years (or DM or CRF) → < 140/90 mmHg
- > 60 years → < 150/90 mmHg

★ **SPRINT**: sBP ≥ 130 mmHg + ≥ 50 years old + increased CV risk (CV disease; GFR 20-60 ml/min; Framingham $> 15\%$ /10-year; ≥ 75 years) + no diabetes / no prior stroke; target \rightarrow sBP < 120 mmHg vs. < 140 mmHg; study terminated prematurely; \searrow MACCE; \searrow Mortality +

NONDRUG TREATMENT: healthy weight (BMI 18.5 to 24.9 kg/m²); waist < 102 cm (M) and < 88 cm (F); regular physical exercise; moderate alcohol consumption; sodium < 2.4 g daily; healthy diet (rich in fruit and vegetables; low-fat; DASH diet); smoking cessation; relaxation techniques

DRUG TREATMENT

- > ★ **ALLHAT**: Chlorthalidone and Lisinopril and Amlodipine are comparable
- > ★ **ASCOT**: Hypertensive patients with ≥ 3 cardiovascular risk factors; Amlodipine + Perindopril superior to Atenolol + Thiazide (study terminated prematurely; \searrow stroke, \searrow mortality)
- > ★ **ACCOMPLISH**: Hypertensive patients with CAD or high risk of CAD; **Benazepril + Amlodipine superior to Benazepril + HCTZ**

ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS

Benazepril	5 mg to 40 mg qd	<ul style="list-style-type: none"> • \nearrow Bradykinin (cough; angioedema) • Accept \nearrow creatinine $\leq 30\%$ • Deterioration of renal function with bilateral renal artery stenosis • Hyperkalemia
Captopril	6.25 mg tid to 50 mg tid	
Cilazapril	1.25 mg to 10 mg qd	
Enalapril	2.5 mg to 40 mg qd	
Fosinopril	10 mg to 40 mg qd	
Lisinopril	5 mg to 40 mg qd	
Perindopril	2.5 to 10 mg qd (2 to 8 mg in Canada)	
Quinalapril	5 mg to 40 mg qd	
Ramipril	1.25 mg to 10 mg qd	
Trandolapril	0.5 mg to 4 mg qd	

ANGIOTENSIN II RECEPTOR BLOCKERS (ARB)

Candesartan	8 mg to 32 mg qd	<ul style="list-style-type: none"> • ARF; Hyperkalemia; OH; Angioedema • Deterioration of renal function with bilateral renal artery stenosis • Do not add ARB to ACE inhibitors (harmful effect in ★ONTARGET)
Irbesartan	75 mg to 300 mg qd	
Losartan	25 to 100 mg qd	
Olmesartan	20 mg to 40 mg qd	
Telmisartan	20 mg to 80 mg qd	
Valsartan	40 mg to 320 mg qd	

DIRECT RENIN INHIBITORS

Aliskiren	150 mg to 300 mg qd	Adverse effect of pro-renin?
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CALCIUM CHANNEL BLOCKERS

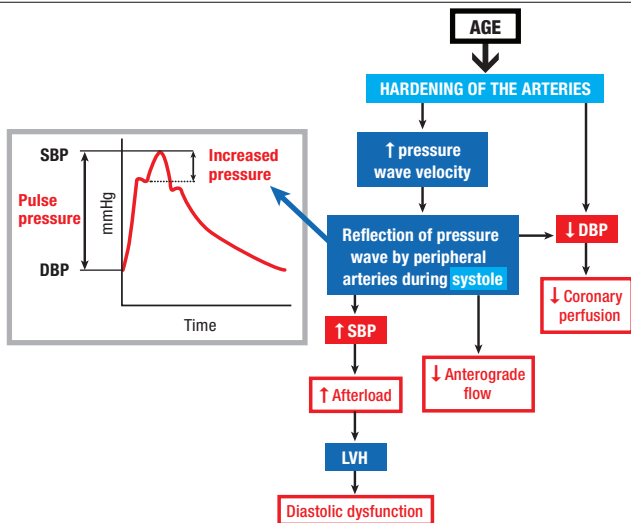
Amlodipine	5 mg to 10 mg qd	<ul style="list-style-type: none"> • Dihydropyridines (Amlodipine and Nifedipine): OH; leg edema; flushing; headache • Non-dihydropyridines (Diltiazem and Verapamil): negative inotropic agent; negative chronotropic agent
Nifedipine	XL: 30 mg to 120 mg qd	
Verapamil	SR: 120 mg qd to 240 mg bid	
Diltiazem	CD: 120 mg to 360 mg qd	

DIURETICS		
Indapamide	1.25-2.5 mg daily	<ul style="list-style-type: none">• Avoid thiazides if CrCl < 30 mL/min• Adverse effects (thiazides): hyponatremia; hypomagnesemia; hypokalemia; OH; glucose intolerance; hypercalcemia; ARF; sulfonamide allergy; gout
Chlorthalidone	12.5-50 mg daily	
Hydrochlorothiazide	6.25-50 mg daily	
Metolazone	2.5-10 mg daily	
Bumetanide	0.5-5 mg daily	
Furosemide	20-600 mg daily	
Torsemide	2.5-10 mg daily	
Eplerenone	25-100 mg daily	
Spironolactone	25-100 mg daily	
Triamterene	50-300 mg daily	
Amiloride	5-10 mg daily	
BETA-BLOCKERS		
Acebutolol	100 mg bid to 400 mg bid	Bronchospasm; Bradycardia; Negative inotropic agent; Exacerbation of PAD; Fatigue; Erectile dysfunction; Rebound effect on withdrawal; Unopposed alpha stimulation (pheochromocytoma); ⬆ TG and ⬆ HDL (nonselective); Masks symptoms of hypoglycemia; glucose intolerance
Atenolol	25 mg to 100 mg qd	
Bisoprolol	2.5 mg to 10 mg qd	
Carvedilol	3.125 mg bid to 50 mg bid	
Labetalol	100 mg bid to 400 mg bid	
Metoprolol	25 mg bid to 100 mg bid	
Nadolol	40 mg to 240 mg qd	
Nebivolol	2.5 mg to 20 mg qd	
Pindolol	2.5 mg bid to 40 mg bid	
Propranolol	LA: 80 mg to 320 mg qd	
Timolol	2.5 mg bid to 20 mg bid	
ALPHA-BLOCKERS		
Doxazosin	1 mg to 16 mg qd	<ul style="list-style-type: none">• Not recommended as first-line• OH; Fluid retention (risk of heart failure)• Doxazosin used as third line in ★ ASCOT
Prazosin	0.5 mg tid to 5 mg tid	
Terazosin	1 mg to 20 mg qd	
CENTRAL ALPHA-ADRENERGIC AGONISTS (VASOMOTOR ACTIVITY CENTER)		
Methyldopa	250-3000 mg daily	Sedation; Dry mouth; Impotence; Galactorrhea; ANA+; Autoimmune anemia
Clonidine	0.1 mg to 0.8 mg bid	Sedation; Dry mouth; Rebound effect on withdrawal

DIRECT VASODILATORS

Hydralazine	10 mg to 50 mg qid	<ul style="list-style-type: none"> • Relaxation of precapillary arterioles • Reflex sympathetic activation; Lupus
Nitroglycerin	Imdur: 60-240 mg / 24h Nitrodur: 0.2 to 0.8 mg/h	Nausea; Headache; Hypotension; Tolerance

HYPERTENSION IN THE ELDERLY



★ **HYVET**: > 80 years; SBP > 160 mmHg; Indapamide / Perindopril vs Placebo; Benefit of treatment (↘ all-cause mortality; ↘ adverse events)

INITIATE TREATMENT IF SBP > 160 mmHG (no RCT with SBP < 160 mmHg)

> **Target** → **SBP ≤ 150 mmHg**

- Caution when DBP < 60 mmHg
- Monitoring of adverse effects: BP supine-standing

PSEUDOHYPERTENSION: HTN on sphygmomanometer, but normal BP on intraarterial measurement; secondary to rigid arteries that are not compressible by the cuff

> **Osler's maneuver**: radial pulse palpable when cuff inflated

TREATMENT-RESISTANT HYPERTENSION

BP > 140/90 mmHg despite ≥ 3 medications at adequate doses (including a diuretic)

ETIOLOGIES: nonadherence; failure to comply with salt restriction; dehydration (↗ stimulation of renin and aldosterone); **insufficient dose of diuretic**; HTN secondary to an underlying cause; hyperaldosteronism; OSAHS

- **Pseudo-resistance: A)** White coat syndrome; **B)** Pseudohypertension in the elderly

MANAGEMENT: Combination of ≥ 3 medications; look for underlying cause; use a sufficient dose of diuretic; mineralocorticoid receptor antagonist; alpha-blocking agent (Doxazosin); percutaneous radiofrequency renal denervation (no benefit in ★ Symplicity HTN-3)

HYPERTENSIVE CRISIS

SBP ≥ 180 MMHG OR DBP ≥ 110 MMHG

HYPERTENSIVE URGENCY: absence of target organ damage

- Often associated with discontinuation of treatment, nonadherence to treatment and/or anxiety
- **Management:** gradual treatment (over 24-48 h); consider oral treatment (Captopril; Furosemide; Propranolol; Nifedipine); avoid target organ hypoperfusion

HYPERTENSIVE EMERGENCY: target organ damage; immediate treatment required; invasive hemodynamic monitoring; target \searrow DBP by 10-15% x 30-60 min

- **Retinal damage:** hemorrhages; exudates; papilledema
- **CNS damage:** Hypertensive encephalopathy (headache; irritability; altered state of consciousness); thrombotic stroke; hemorrhagic stroke; SAH
 - **Cerebral autoregulation:** \nearrow intracerebral blood pressure when DBP > 110-130 mmHg (autoregulatory mechanisms no longer effective); risk of cerebral edema
- **Cardiac damage:** Aortic dissection; acute heart failure; acute coronary syndrome
- **Renal damage:** ARF
- **Other:** Eclampsia / HELLP syndrome; Microangiopathic hemolytic anemia

Nitroprusside	IV infusion: 0.25-10 μ g/kg/min (short duration)	Nausea; Vomiting; Cyanide toxicity; Avoid in the presence of CNS damage or ARF or liver failure
	Standard dilution: 50 mg/250 mL D5 %	
IV Nitroglycerin	Perfusion: 5-60 μ g/min	Headache; Vomiting; Methemoglobinemia; Tolerance
	Standard dilution: 50 mg/250 mL D5 %	
Labetalol	<ul style="list-style-type: none"> • IV bolus: 20-80 mg every 10 min • IV infusion: 2 mg/min (max 300 mg / 24 h) 	Vomiting; Faintness; Nausea; Block; OH
	Standard dilution: 200 mg/160 mL NS (= 1 mg/mL)	
Esmolol	<ul style="list-style-type: none"> • Bolus: 0.25-0.5 mg/kg/min x 4 min • IV infusion: 0.05-0.3 mg/kg/min 	Hypotension; Nausea; Block
	Standard dilution: 2500 mg/250 mL	
IV Nicardipine	IV infusion: 5-15 mg/h	Headache; Nausea; Flushing; Tachycardia

9.6/ DIABETES

TYPE 1 DM: autoimmune (or idiopathic) destruction of pancreatic beta cells

TYPE 2 DM: insulin resistance and/or abnormal insulin secretion

DIAGNOSIS

DIAGNOSIS OF DIABETES	PREDIABETES		
	Abnormal fasting blood glucose	Glucose intolerance	Prediabetes
<ul style="list-style-type: none"> • Fasting blood glucose: ≥ 7.0 mmol/L (≥ 126 mg/dL) or • Random blood glucose: ≥ 11.1 mmol/L (≥ 200 mg/dL) or • Blood glucose 2 h after 75 g glucose load: ≥ 11.1 mmol/L or • HbA1c: $\geq 6.5\%$ 	Fasting blood glucose: 6.1 - 6.9 mmol/L (110 - 124 mg/dL) Rule out Glucose intolerance	Blood glucose 2 h after 75 g glucose load: 7.8 - 11.0 mmol/L (140 - 200 mg/dL)	HbA1c: 6.0 - 6.4% Rule out Glucose intolerance
	More intensive management of cardiovascular risk factors; consider Metformin or Acarbose		

GLYCEMIC CONTROL - TYPE II DIABETES

BENEFITS OF GLYCEMIC CONTROL

- **Reduction of microvascular complications:** retinopathy; nephropathy; neuropathy (★ DCCT - ★ UKPDS - ★ ADVANCE)
- **Little evidence concerning the benefit on macrovascular complications:**
★ ADVANCE and ★ VADT; ★ ACCORD demonstrated excess mortality for target HbA1c < 6%

GLYCEMIC CONTROL TARGETS		
HbA1c	Fasting blood glucose & Preprandial blood glucose	2 h postprandial blood glucose
$\leq 7\%$ every 3 months (every 6 months when target achieved)	4.0 - 7.0 mmol/L (72 - 126 mg/dL)	5.0 - 10.0 mmol/L (5.0 - 8.0 when target HbA1c not achieved)

- 1) NONDRUG TREATMENT:** weight loss (< 5%); balanced diet / follow-up by a nutritionist; regular moderate aerobic physical exercise (30 min; 5 times a week)
 - **Stress test prior to training program:** consider in patients at high-risk of cardiovascular disease (or with microvascular complication) in the case of training with an intensity greater than rapid walking
- 2) FIRST-LINE DRUG TREATMENT:** Metformin
- 3) SECOND-LINE DRUG TREATMENT:** in combination with Metformin
 - Sulfonylurea (or Meglitinide) and/or Incretins
 - Bedtime basal insulin therapy
- 4) INSULIN THERAPY:** 3 approaches
 - a) Bedtime basal insulin therapy:** combined with oral antidiabetic; **starting dose of 10 units at bedtime;** increase by 1 unit per day, targeting a fasting blood glucose of 4.0-7.0 mmol/L (72 - 126 mg/dL); avoid nocturnal hypoglycemia
 - b) Premixed insulin:** **starting dose of 5-10 units bid** (before breakfast and before dinner); increase the morning dose by 1 unit, targeting evening blood glucose before dinner of 4.0 - 7.0 mmol/L (idem for the evening dose, targeting morning fasting blood glucose of 4.0 - 7.0 mmol/L)
 - c) Intensive insulin therapy:** **total daily dose = 0.3 to 0.5 kg unit;** 40% of the total dose as bedtime basal insulin therapy; 20% of the total dose as bolus doses tid with each meal

Biguanide	Metformin: 250 mg bid to 850 mg tid	Decreases hepatic glucose synthesis	<p>↘ HbA1c by 0.8%</p> <p>Adverse effects: Nausea; Diarrhea; Lactic acidosis (contraindicated if GFR < 30 mL/min)</p> <p>Weight loss</p> <p>Benefit on the risk of MI and mortality in obese patients in ★ UKPDS</p>
Sulfonylureas	<ul style="list-style-type: none"> Gliclazide: 60 mg qd to 120 mg qd Glimepiride: 1 to 8 mg qd Glyburide: 2.5 mg qd to 10 mg bid 	Stimulates insulin secretion by the pancreas	<p>↘ HbA1c by 0.7%</p> <p>Adverse effects: Hypoglycemia (prefer Gliclazide which is associated with the lowest risk of hypoglycemia); weight gain</p> <p>Benefit on the risk of MI in ★ UKPDS</p>
Meglitinide	Repaglinide: 0.5 mg tid to 4 mg qid	Stimulates insulin secretion by the pancreas	<p>↘ HbA1c by 1-1.5 %</p> <p>Short duration of action (to be taken < 30 min before the meal)</p> <p>Adverse effects: Hypoglycemia; Weight gain</p>
Incretin - GLP-1 analog ("glucagon-like peptide 1")	<ul style="list-style-type: none"> Exenatide: 5 to 10 µg SC bid Liraglutide: 0.6 to 1.8 mg SC daily 	<p>GLP-1:</p> <ul style="list-style-type: none"> ↗ insulin secretion; ↘ glucagon secretion; delays gastric emptying 	<p>↘ HbA1c by 1 %</p> <p>Weight loss</p> <p>Adverse effects: Nausea; Vomiting</p>
Incretin - DPP-4 inhibitors	<ul style="list-style-type: none"> Sitagliptin: 100 mg qd Linagliptin: 5 mg qd Saxagliptin: 5 mg qd 	Inhibits the breakdown of GLP-1	<p>↘ HbA1c by 0.7 %</p> <p>Safe post-ACS (★EXAMINE; Alogliptin)</p> <p>Adverse effects:</p> <ul style="list-style-type: none"> ↗ hospitalization for heart failure with Saxagliptin in ★SAVOR but not with Sitagliptin in ★TECOS
Alpha-glucosidase inhibitor	Acarbose: 25 mg tid to 100 mg tid	Decreases intestinal absorption of carbohydrates	<p>↘ HbA1c by 0.6 %</p> <p>Adverse effects: Bloating</p>
Thiazolidinedione (TZD)	Pioglitazone: 15 mg to 45 mg qd	Increases peripheral insulin sensitivity	<p>↘ HbA1c by 0.8 %</p> <p>Adverse effects: Weight gain; Edema; contraindicated in heart failure (★ DREAM); bladder tumor; fracture</p>

SGLT2 inhibitors	Canagliflozin Dapagliflozin Empagliflozin	↘ glucose reabsorption by the renal proximal tubule	↘ All-cause mortality with Empagliflozin in ★ EMPA-REG ↘ BP; Weight loss Adverse effects: urinary tract infections; candidiasis; ↗ LDL
RAPID ACTING INSULIN	• Aspart (NovoRapid) • Lispro (Humalog)	• Onset of action: 10-15 min • Peak action: 1-2 h • Duration of action: 3-5 h	
REGULAR INSULIN	• Humulin-R • Novolin ge Toronto	• Onset of action: 30 min • Peak action: 2-3 h • Duration of action: 6.5 h	
INTERMEDIATE-ACTING INSULIN	• Humulin-N • Novolin ge NPH	• Onset of action: 1-3 h • Peak of action: 5-8 h • Duration of action: up to 17 h	
LONG-ACTING INSULIN	• Detemir (Levemir) • Glargine (Lantus)	• Onset of action: 90 min • Duration of action: up to 24 h	
PREMIXED INSULIN	Humulin 30/70; Novolin ge 30/70; Biphasic insulin aspart (NovoMix 30); Insulin lispro / lispro protamine (Humalog Mix25)...		

MANAGEMENT - TYPE II DIABETES

CARDIOVASCULAR RISK: 2- to 3-fold higher prevalence of coronary artery disease than in nondiabetic subjects; coronary artery disease occurs 10 years earlier

CONTROL OF CARDIOVASCULAR RISK FACTORS: healthy weight; waist < 102 cm (M) and < 88 cm (F); BMI 18.5 - 24.9 kg/m²; healthy diet; regular physical exercise; smoking cessation

CONTROL BP: target BP < 140/85 and prefer ACEi (or ARB) as first-line treatment

- ★ **ACCORD-BP:** no benefit of targeting SBP < 120 versus < 140 mmHg

ANTIPLATELET THERAPY (ASA):

- **Secondary prevention:** indicated for all patients
 ➤ **Primary prevention:** uncertain benefit (ongoing ★ ASCEND and ★ ACCEPT-D studies); not recommended routinely; consider if high 10-year risk of cardiovascular events in the absence of bleeding risk (class IIb recommendation); **decision based on clinical judgment** +

STATIN: ★ CARDS and ★ HPS studies of primary prevention demonstrated a benefit

- **European guidelines - Indications: A)** Very high risk → DMI or DMII + (macrovascular disease or CRF ≥ 3/5 or cardiovascular risk factors or microvascular complication); **B)** High risk → DMII + (absence of cardiovascular risk factors and absence of target organ damage)
 ➤ **Canadian guidelines - Indications:** Diabetes + (≥ 40 years or present for > 15 years in a patient ≥ 30 years or macrovascular disease or microvascular complication)
 ➤ **American guidelines - Indications:** Diabetes + 40-75 years + LDL ≥ 70 mg/dL (≥ 1.8 mmol/L)

ACEI: cardioprotective effect: (★ HOPE, ★ EUROPA and ★ ADVANCE); indicated in the presence of HTN or clinical macrovascular disease or ≥ 55 years or in the presence of a microvascular complication

- **ARB:** when ACEi are not tolerated; ★ ONTARGET → Telmisartan non-inferior to Ramipril;
 ★ TRANSCEND → no benefit of Telmisartan versus placebo (patients intolerant to ACEi)

NONINVASIVE ASSESSMENT OF CAD (PROGNOSTIC PURPOSES): Indications → **A)** Symptoms (retrosternal chest pain; dyspnea); **B)** Baseline ECG abnormalities; **C)** Atherosclerosis (PAD - TIA - stroke - murmur)

- **Revascularization: benefit of revascularization by bypass graft (versus PCI) on mortality and risk of MI (★ FREEDOM)** +

VACCINATION: Influenza (annually); Pneumococcus

OTHER: self-monitoring of blood glucose; screening for retinopathy (every 1-2 years); screening for neuropathy (big toe; Semmes-Weinstein 10 g monofilament test or 128 Hz tuning fork); examination of feet; prevention of diabetic ulcer; PDE-5 inhibitor for erectile dysfunction

HYPOGLYCEMIA: Blood glucose < 4 mmol/L (72 mg/dL) + symptoms (tremor; palpitations; anxiety; profuse sweating; nausea; confusion; weakness); **treatment with 15 g of oral carbohydrate or 1 mg of Glucagon SC (or IM) or 1 ampoule of 50% dextrose IV**

DIABETIC NEPHROPATHY

CHRONIC NEPHROPATHY: GFR < 60 mL/min and/or microalbuminuria or macroalbuminuria

SCREENING: albumin / creatinine ratio and serum creatinine (and GFR) every year

MANAGEMENT: optimal control of blood glucose and BP; ACEi or ARB; Nephrological follow-up if sustained deterioration or GFR < 30 mL/min or significant macroalbuminuria; aggressive treatment of cardiovascular risk factors (high risk of adverse events)

ALBUMINURIA			NEPHROPATHY		
	Albumin / creatinine ratio (mg/mmol)	Albumin mg / 24h	Stage	Renal damage	GFR (mL/min)
Normal	< 2.0	< 30	1	Minimal - Absent	≥ 90
Micro-albuminuria	2.0 - 20.0	30 - 300	2	Mild	60 - 89
Macro-albuminuria	> 20.0	> 300	3	Moderate	30 - 59
			4	Severe	15 - 29
			5	End-stage	< 15

9.7/ PHYSICAL ACTIVITY

PHYSIOLOGY OF EXERCISE

- **CARDIAC OUTPUT:** ➤ up to 4- to 6-fold
 - **Stroke volume** (➤ venous return → Frank-Starling law; catecholamines → positive inotropes)
 - **HR** (HRmax ≈ 220 - age)
- **REDISTRIBUTION OF PERFUSION:** vasodilatation in muscles; vasoconstriction of other systems (except for CNS and heart)
- **O₂ EXTRACTION BY MUSCLES**
- **CORONARY PERFUSION:** ➤ up to fivefold; vasodilatation of coronary arterioles
 - **MVO₂:** myocardial O₂ consumption; determined by **HR / SBP / LV end-diastolic volume / wall thickness / contractility** +

BENEFITS & RISKS

BENEFITS OF EXERCISE ON CONVENTIONAL CARDIOVASCULAR RISK FACTORS

- **HTN:** ↘ 3.4 / 2.4 mmHg
- **Dyslipidemia:** ↗ HDL 0.06 mmol/L (2.3 mg/dL); ↘ TG
- **Obesity:** ↘ 7 kg in 1 year (in combination with diet)
- **Diabetes:** ↘ HbA1c by 0.8%

IMPROVEMENT OF OTHER PARAMETERS: functional capacity; quality of life; mental health; endothelial function; inflammatory state; ischemic threshold

- **Physical activity:** ↘ mortality and ↘ cardiovascular events in patients with CAD (meta-analyses); ↘ mortality and hospitalizations in patients with LVEF < 35% (★ HF-ACTION; after adjustments)

BENEFITS OF TRAINING: ↗ $\dot{V}O_2$ max; ↗ stroke volume; lower HR for the same level of exercise (same HRmax); ↗ arteriovenous O_2 difference; delayed ventilatory threshold; ↘ $\dot{M}VO_2$ for the same level of exercise

RISKS OF PHYSICAL EXERCISE

- a) < 35 years:** sudden death / arrhythmia / genetic condition (HCM; congenital coronary artery anomalies; myocarditis; ARVD; Channelopathy; CAD; Acute aortic syndrome; Aortic stenosis; DCM; WPW; *commotio cordis*)
- b) > 35 years:** CAD / MI (especially in sedentary subject performing unusually strenuous exercise)

INTENSITY OF PHYSICAL EXERCISE

1 MET: = O_2 consumption at rest while seated (3.5 mL O_2 /kg/min)

< 3 METs	3 - 5 METs	5 - 7 METs	7 - 9 METs	> 9 METs
<ul style="list-style-type: none"> • Washing • Shaving • Dressing • Washing the dishes • Sewing • Playing a musical instrument • Golf (caddy) • Walking (3.2 kph) • Fishing • Pool 	<ul style="list-style-type: none"> • Washing the windows • Electric lawnmower • Making a bed • Dancing • Golf • Sailing • Tennis (doubles) • Volleyball (6 players) • Ping-pong • Walking (6.4 kph) 	<ul style="list-style-type: none"> • Manual lawnmower • Climbing stairs (slowly) • Badminton • Tennis (singles) • Basketball • Walking (8 kph) • Bike-riding (16 kph) • Swimming (breaststroke) 	<ul style="list-style-type: none"> • Shoveling snow • Climbing stairs (moderate speed) • Canoe • Soccer • Jogging (8 kph) • Swimming (front crawl) • Bike-riding (19 kph) • Mountain-climbing 	<ul style="list-style-type: none"> • Climbing stairs (rapidly) • Shoveling heavy snow • Handball • Squash • Running (> 10 kph) • Bike-riding (> 21 kph)

EVALUATION OF THE RISK OF PHYSICAL EXERCISE

PRE-TRAINING STRESS TEST: **A)** DM; **B)** Symptoms or multiple cardiovascular risk factors or known heart disease; **C)** Strenuous physical exercise by a sedentary subject (M > 45 years and F > 55 years)

CATEGORY	CHARACTERISTICS	MANAGEMENT
Class A: In good health	<ul style="list-style-type: none"> • M < 45 years or F < 55 years with no symptoms, no heart disease and no major cardiovascular risk factors • M > 45 years or F > 55 years with no symptoms, no heart disease and ≤ 1 major cardiovascular risk factor • M > 45 or F > 55 years with no symptoms, no heart disease with ≥ 2 major cardiovascular risk factors 	<ul style="list-style-type: none"> • No restriction • No supervision required • Physical examination / Stress test as necessary (according to cardiovascular risk factors / type of strenuous exercise)
Class B: Stable heart disease	<ul style="list-style-type: none"> • Stable CAD • Nonsevere valvular heart disease • Stable congenital heart disease (according to 36th Bethesda conference) • Stable cardiomyopathy (LVEF ≤ 30%) • Abnormal stress test (no class C abnormalities) <p style="text-align: center;">+</p> <p style="text-align: center;">CLINICAL CHARACTERISTICS</p> <p>NYHA I or II; No decompensated heart failure; ≥ 6 METs; No ischemia < 6 METs; Normal BP response to exercise; No VT on effort - rest; Able to selfmonitor</p>	<ul style="list-style-type: none"> • Individualized prescription (50% of HR reserve then increase) • Medical supervision with monitoring during the initial phase (6-12 sessions) • Nonmedical supervision thereafter until the patient is able to self-monitor
Class C: Moderate to high risk	<ul style="list-style-type: none"> • CAD • Nonsevere valvular heart disease • Moderate congenital heart disease (36th Bethesda conference) • Cardiomyopathy (LVEF ≤ 30%) • Partially controlled ventricular arrhythmia <p style="text-align: center;">+</p> <p style="text-align: center;">CLINICAL CHARACTERISTICS</p> <p>NYHA III-IV; Stress test < 6 METs; Ischemia < 6 METs; Abnormal BP response to exercise; NSVT on exercise; History of cardiac arrest; Potentially dangerous medical condition</p>	<ul style="list-style-type: none"> • Individualized prescription (40% of HR reserve then increase) • Medical supervision with monitoring until safety is confirmed (> 12 sessions) • Can be classified as class B when exercise is safe
Class D: Unstable condition	<ul style="list-style-type: none"> • Unstable ischemia • Severe valvular heart disease / symptoms • Severe congenital heart disease • Decompensated heart failure • Uncontrolled arrhythmia • Other condition worsened by exercise 	<ul style="list-style-type: none"> • Exercise contraindicated • Target treatment of the disease

Fletcher GF, Balady GJ, Amsterdam EA. Exercise Standards for Testing and Training; A Statement for Healthcare Professionals From the American Heart Association. *Circulation*. 2001;104:1694-1740

COMPETITIVE SPORT: according to the 36th Bethesda conference

PRESCRIPTION OF AEROBIC (ISOTONIC) PHYSICAL EXERCISE

FREQUENCY: 5 times a week

DURATION: 30 min (in 10-min fractions if necessary)

INTENSITY: moderate

- **Target:** ideally 450 to 750 METs x min / week (1000 kcal / week)
- **Kcal/min:** = (METs x 3.5 x kg weight) / 200
- **Strenuous aerobic exercise:** 3 times a week; 20 min per session

MODERATE AEROBIC EXERCISE	VIGOROUS AEROBIC EXERCISE
<ul style="list-style-type: none"> • % VO₂ max: 45-59 % • % HR reserve: 45-59 % • % HRmax: 55-69 % • Borg scale: 12-13 / 20 Comfortable while talking (≈ ventilatory threshold ≈ 50 % VO₂Max) • METs: 4 - 6 METs (middle-aged) 5 - 7 METs (young) 3 - 5 METs (elderly) 2 - 3 METs (very elderly) • Type of exercise: rapid walking; bike-riding; swimming; dancing; pool aerobics; elliptic exercise machine 	<ul style="list-style-type: none"> • % VO₂ max: 60-85 % • % HR reserve: 60-85 % • % HRmax: 70-90 % • Borg scale: 14-16 / 20 Conversation is difficult during exercise • METs: 6 - 8.5 METs (middle-aged) 7 - 10 METs (young) 5 - 7 METs (elderly) 3 - 4 METs (very elderly) • Type of exercise: rapid walking uphill; jogging; rapid swimming; hockey; singles tennis; shoveling snow
<ul style="list-style-type: none"> • Target HR according to HR reserve: = (prescribed % x HR reserve) + resting HR • HR reserve: = HRmax on stress test - resting HR • HRmax: = 220 - age • HRmax: = HRmax on stress test limited by symptoms 	
<ul style="list-style-type: none"> • Ischemia on stress test: Target HR on exercise must be at least 10 bpm lower than ischemic threshold (or target HR = 70% of HR at the ischemic threshold) 	

PRESCRIPTION OF RESISTANCE TRAINING (STATIC; ISOMETRIC)

FREQUENCY: twice a week

CONTENT: 1-3 series of 8 to 12 repetitions of the prescribed load (counterweight machine or dumbbells)

8-10 MUSCLE GROUPS: Biceps; Triceps; Shoulders; Pectorals; Back; Abdominal muscles; Leg muscles

PRESCRIBED LOAD: maximum load that can be lifted once → 35% of this maximum load for arms and 45% for legs

9.8/ WEIGHT & DIET

WEIGHT CONTROL

BMI: = Mass (kg) / Height ² (m²)

Underweight	BMI < 18.5 kg/m ²
Healthy weight	BMI 18.5 - 24.9 kg/m ²
Overweight	BMI 25.0 - 29.9 kg/m ²
Obesity - Class I	BMI 30.0 - 34.9 kg/m ²
Obesity - Class II	BMI 35.0 - 39.9 kg/m ²
Obesity - Class III (morbid)	BMI ≥ 40 kg/m ²

BENEFIT OF WEIGHT CONTROL ON CARDIOVASCULAR RISK FACTORS: ↓ BP; improves lipid profile (↓ TG; ↓ atherogenic lipoproteins; ↑ HDL); ↓ DM; ↓ OSAHS; ↓ inflammatory state; improves endothelial function

WEIGHT LOSS

BMI	Target 18.5 - 24.9 kg/m ²
WAIST (midpoint between superior iliac crest and costal margin)	Target < 102 cm M and < 88 cm F (ideally < 94 cm M and < 80 cm F)

1) LIFESTYLE MODIFICATION: healthy diet; regular physical exercise; behavioral therapy (selfmonitoring; eat more slowly; eat smaller servings; nutritional education...)

- **Targets:** weight loss of 5% in 3-6 months (realistic target)
- **Measurements:** energy deficit of 500 kcal per day (loss of 1-2 pounds per week); Regular exercise program (30 min; 5 times a week)

2) DRUG TREATMENT: indicated after failure of nondrug treatment for 6 months with BMI > 30 kg/m² (or > 27 kg/m² with comorbidities)

Pancreatic lipase inhibitor	Orlistat 120 mg tid + fat-soluble vitamin supplement	Inhibits digestion and absorption of dietary fat by 30%	Bloating; Steatorrhea; Abdominal cramps; Renal stones
Selective serotonin agonist	Lorcaserin	Early satiety	Faintness; Nausea; Headache; URTI; Uncertain long-term safety (valvular heart disease?)

3) BARIATRIC SURGERY: indicated in the presence of class III obesity (or class II obesity with secondary comorbidities) and failure of other treatment modalities with an acceptable operative risk

- **Options:** Vertical gastropasty with laparoscopic banding or laparoscopic Roux-en-Y gastric bypass

HEALTHY DIET

DASH diet or Mediterranean diet or AHA diet; emphasize intake of vegetables, fruits, whole grains, nontropical vegetable oils, nuts, low-fat dairy products, fish, poultry; limit intake of sodium - sweets - sugar-sweetened beverages - red meats

BENEFIT ON CONVENTIONAL CARDIOVASCULAR RISK FACTORS: ↓ LDL; ↓ BP; ↓ Weight; ↓ DM

MEDITERRANEAN DIET: rich in olive oil / nuts / fruit and vegetables; ↘ cardiovascular mortality in secondary prevention (★ Lyon diet heart study) and ↘ cardiovascular events in primary prevention (★ PREDIMED)

Total calories - Energy balance	Intake equal to energy expenditure Normal intake: 22 kcal/kg (± 20%)
Fat	< 35 % of total energy intake
Mono- and polyunsaturated fatty acids (fish; vegetable oils; nuts)	<ul style="list-style-type: none"> • Increase intake • Omega-3 fatty acids → ↘ cardiovascular mortality (★ GISSI-Prevention)
Saturated fatty acids	< 7% of total energy intake Avoid red meat - high-fat dairy products - tropical oils (palm; coconut)
Trans fatty acids / Hydrogenated oils	Limit to a minimum; < 1% of total energy intake; ↗ LDL and ↘ HDL
Dietary cholesterol	< 200-300 mg daily
Carbohydrates	45 - 60% of total energy intake Prefer whole grain products - low-fat dairy products - fruit and vegetables Avoid carbohydrates with a high glycemic index (potatoes; white bread; white rice; soft drinks)
Proteins	15 - 20% of total energy intake
Fibers (whole grains; fruit; vegetables; nuts)	Increase intake; 25 - 50 g daily
Fruit and vegetables	≥ 8-10 servings per day
Fish	At least twice a week
Sodium	< 2.4 g per day
Alcohol	M: 20 g per day (2 glasses); F: 10 g per day (1 glass) (caution in the presence of DM - HTN - Liver disease - History of alcohol abuse)
Red meat; High-fat dairy products	Limit to a minimum

METABOLIC SYNDROME

CENTRAL OBESITY (WAIST) USA - Canada: M: ≥ 102 cm; F: ≥ 88 cm Europid: M: ≥ 94 cm; F: ≥ 80 cm	+	≥ 2 OF THE FOLLOWING RISK FACTORS <ul style="list-style-type: none"> • TG ≥ 1.7 mmol/L (150 mg/dL) • HDL: M < 1.03 and F < 1.3 mmol/L (40 - 50 mg/dL) • BP ≥ 130/85 (or treated HTN) • Fasting blood glucose ≥ 5.6 mmol/L (100 mg/dL)
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↗ risk of cardiovascular disease and DMII

MANAGEMENT: control of cardiovascular risk factor; regular exercise; weight loss

9.9/ OBSTRUCTIVE SLEEP APNEA SYNDROME

OBSTRUCTIVE APNEA: absence of airflow for ≥ 10 s despite active ventilatory efforts

OBSTRUCTIVE HYPOPNEA: ↘ airflow < 50% for ≥ 10 s with ↘ SaO₂ ≥ 4 %

APNEA-HYPOPNEA INDEX (AHI): mean number of episodes of apnea and hypopnea per hour (mild if AHI ≥ 5 ; severe if AHI ≥ 30)

CLINICAL FEATURES: snoring; daytime sleepiness; witnessed apnea during the night; morning headache; disorders of concentration

HARMFUL EFFECTS: sympathetic stimulation; transient hypoxemia; marked fluctuations of intrathoracic pressure (\nearrow afterload); nocturnal HTN; treatment-resistant HTN; diastolic dysfunction; nocturnal angina

ASSOCIATIONS: obesity; DM; metabolic syndrome; AF; CAD; stroke; heart failure; nonischemic dilated cardiomyopathy; PHT

DIAGNOSIS: Polysomnography (screening by nocturnal saturimetry)

TREATMENT: Weight loss; CPAP; Oral device; Surgery

9.10/ DRIVING & AIR TRAVEL

	PRIVATE VEHICLE	COMMERCIAL VEHICLE
STEMI	1 month	3 months
NSTEMI - Significant damage (RWMA)	1 month	3 months
Unstable angina or NSTEMI without RWMA	48 h post-PCI (7 days in the absence of PCI)	7 days post-PCI (30 days in the absence of PCI)
CAD - PCI	48 h post-PCI	7 days post-PCI
CABG	1 month	3 months
LMCA	Disqualified if > 70%	Disqualified if > 50%
VF - Absence of reversible cause	6 months	Disqualified
Unstable VT	6 months	Disqualified
VT or VF - Reversible cause (MI; Electrocuting; Drugs)	Disqualified until correction of reversible cause	
Stable sustained VT - LVEF < 30%	3 months	Disqualified
Stable sustained VT - LVEF \geq 30%; without ICD	4 weeks	3 months
Symptomatic SSS	Disqualified until treatment	
LBBB or Bifascicular block or Mobitz I or Bifascicular block + 1st degree AV block	No restriction in the absence of alteration of LOC	No restriction in the absence of alteration of LOC and in the absence of higher grade of AV block on annual Holter
Mobitz II (infranodal)	Disqualified	Disqualified
Alternating RBBB and LBBB	Disqualified	Disqualified
3rd degree AV block	Disqualified	Disqualified

Pacemaker	1 week post-implantation (no alteration of LOC postimplantation; functioning pacemaker)	1 month post-implantation (no alteration of LOC postimplantation; functioning pacemaker)
ICD - Primary prevention (NYHA I to III)	4 weeks	Disqualified
ICD - Secondary prevention (VF or VT with alteration of LOC)	6 months	
ICD - Secondary prevention (stable VT; NYHA I to III)	1 week + interval associated with VT	
Therapy (ATP or shock) with alteration of LOC	6 months	
Brugada / Long QT / ARVD	6 months after episode with alteration of LOC	Disqualified
EPS (without induced VT) or ablation procedure	48 h	1 week
SVT / AF / Flutter with alteration of LOC	<ul style="list-style-type: none"> • Ablation: 48 h • Medical treatment: 3 months 	<ul style="list-style-type: none"> • Ablation: 1 week • Medical treatment: 3 months
Classical vasovagal syncope - 1st episode	No restriction	No restriction
Classical vasovagal syncope - Recurrence (< 12 months)	1 week	12 months
Syncope with treated cause (e.g.: pacemaker)	1 week	1 months
Situational syncope	1 week	1 week
Unexplained syncope - 1st episode	1 week	12 months
Unexplained syncope - Recurrence (< 12 months)	3 months	12 months
AS	NYHA I or II; No alteration of LOC	Asymptomatic - NYHA I - Area $\geq 1 \text{ cm}^2$ - LVEF $\geq 35\%$
AR - MS - MR	NYHA I or II; No alteration of LOC	No alteration of LOC - NYHA I - LVEF $\geq 35\%$
Mechanical valve or Bioprosthesis	6 weeks Anticoagulation (if indicated) No thromboembolic complication	3 months NYHA I and LVEF $\geq 35\%$ Anticoagulation (if indicated) No thromboembolic complication
NYHA I or II	No restriction	LVEF $\geq 35\%$
NYHA III	No restriction	Disqualified
NYHA IV	Disqualified	Disqualified

Heart transplant	6 week NYHA I or II	6 months NYHA I; LVEF \geq 35% No ischemia on annual noninvasive test
LVAD - continuous flow ventricular assist device	2 months NYHA I-III	Disqualified
HCM	No alteration of LOC	Wall thickness $<$ 30 mm; No syncope; No NSVT (annual Holter); No family history of sudden death; No \searrow BP on exercise

AIR TRAVEL

INDICATION FOR O₂: **A)** PaO₂ $<$ 70 mmHg; **B)** CCS III/IV angina; **C)** NYHA III/IV heart failure; **D)** Cyanotic congenital heart disease; **E)** PHT - Right heart failure

Stable angina / NYHA I - II - III	O ₂ if NYHA III
Post-myocardial infarction / NYHA I	6-8 weeks
Heart failure / NYHA I - II - III	O ₂ if NYHA III
Valvular heart disease / NYHA I - II - III	O ₂ if NYHA III or PHT
Congenital heart disease / NYHA I - II - III	O ₂ if NYHA III or PHT or PaO ₂ $<$ 70 mmHg
ICD / NYHA I - II	1 month post-ICD therapy associated with presyncope or syncope

9.11/ CARDIOVASCULAR COMPLICATIONS OF SYSTEMIC DISEASES

HIV

Heart failure - Dilated cardiomyopathy - Myocarditis; Pericardial effusion / Pericarditis; Infective and noninfective endocarditis (non-bacterial thrombotic endocarditis); PHT; Neoplasia \rightarrow Kaposi sarcoma (epicardial) / NHL; Accelerated atherosclerosis / Endothelial dysfunction; Early-onset cerebrovascular disease; Protease inhibitors \rightarrow lipodystrophy / \nearrow TG - \nearrow LDL - \searrow HDL / Glucose intolerance; Arrhythmias - \nearrow QT; Dysautonomia; Vasculitis; Drug interactions

VASCULITIS

TAKAYASU - GIANT CELL ARTERITIS - BEHÇET: \gg Chapter 8

KAWASAKI: young children ($<$ 5 years); fever; rash; conjunctivitis; lymphadenopathy; mucosal lesions; erythema of extremities then desquamation

- \triangleright **Cardiac involvement:** pericardial effusion; myocarditis; MI; aortitis; AR; heart failure; arrhythmias; coronary arteritis
- \triangleright **Coronary artery stenoses or aneurysms:** $<$ 6 weeks after onset of the disease; proximal lesions; short-term, medium-term and long-term risk of thrombosis
- \triangleright **Treatment:** ASA; IV Ig; consider anticoagulation if multiple aneurysms or thrombus

CHURG & STRAUSS: pericarditis; myocarditis; coronary arteritis; heart failure; mesenteric ischemia

POLYARTERITIS NODOSA (MEDIUM VESSEL VASCULITIS): HTN; heart failure; arteritis; coronary aneurysms; angina; myocardial infarction; pericarditis

CONNECTIVE TISSUE DISEASES

RHEUMATOID ARTHRITIS: pericarditis; pericardial effusion; constriction; accelerated CAD; blocks (rheumatoid nodules); granulomatous valve lesions with regurgitation (mitral; aortic); rheumatoid aortitis; PHT (rheumatoid lung disease)

HLA-B27-ASSOCIATED SPONDYLOARTHROPATHIES: aortitis / aortic root dilatation; aortic valvulitis; AR; blocks; early CAD

SYSTEMIC LUPUS ERYTHEMATOSUS: pericarditis; pericardial effusion; constrictive pericarditis; coronary arteritis; accelerated CAD; nonbacterial endocarditis (Libman-Sacks; nonmobile vegetations); valvulitis (fibrosis; retraction; regurgitation); myocarditis; sinus tachycardia; congenital AV block; PHT; aortitis

➤ **Drug-induced lupus:** hydralazine; procainamide; quinidine

➤ **Antiphospholipid syndrome (antiphospholipid antibodies or lupus anticoagulant):** arterial or venous thrombosis; myocardial infarction; stroke; intracardiac thrombus; PHT; nonbacterial endocarditis; valvulitis (fibrosis; regurgitation)

SCLERODERMA: Raynaud; renal crisis; pericarditis; pericardial effusion; microvascular ischemia; myocardial fibrosis; heart failure (diastolic > systolic); conduction disorders; PHT

POLYMYOSITIS: myocarditis / heart failure; blocks; PHT

ENDOCRINE DISEASES

ACROMEGALY: HTN; LVH; heart failure; diastolic dysfunction; stroke; insulin resistance; aortic root dilatation; mitral regurgitation

CUSHING'S DISEASE: Accelerated CAD; hyperglycemia / insulin resistance; dyslipidemia; HTN; LVH; heart failure; dilated cardiomyopathy; stroke; PAD

HYPERPARATHYROIDISM: ⚡ contractility; short QT; calcifications (valvular; aortic)

HYPOCALCEMIA: Prolonged QT; ⚡ contractility

HYPERTHYROIDISM: high output; ⚡ systemic resistance; systolic HTN (⚡ pulse pressure); sinus tachycardia; ⚡ plasma volume; angina (⚡ O₂ demand); vasospasm; PHT; AF; heart failure

HYPOTHYROIDISM: low output state; ⚡ systemic resistance; sinus bradycardia; diastolic HTN; ⚡ LDL; hypertriglyceridemia; pericardial effusion; prolonged QT; low voltage; ⚡ risk of CAD; diastolic dysfunction

PHEOCHROMOCYTOMA: HTN; tachycardia; concentric LVH; myocarditis; cardiomyopathy similar to Takotsubo

MUSCULAR DYSTROPHIES

PERMANENT PACEMAKER: **A)** Third-degree or advanced second-degree AV block (class I recommendation); **B)** May be considered with any degree of AV block (including first degree) in patients with Steinert disease, Kearns-Sayre syndrome or limb-girdle muscular dystrophy (class IIb)

BECKER DYSTROPHY AND DUCHENNE DYSTROPHY: X-linked; ⚡ CK; **progressive dilated cardiomyopathy;** MR; hypertrabeculations; arrhythmias; blocks

➤ **Duchenne:** prominent R wave in V1 (⚡ R/S ratio); Q wave in left precordials; short PR; RVH

MYOTONIC DYSTROPHY: autosomal dominant; **predominantly affects conduction tissue**; blocks; arrhythmias (AF; flutter; VT; bundle branch reentry VT); systolic and/or diastolic dysfunction; LVH; MVP

➤ **Follow-up:** Annual ECG and Holter

EMERY-DREIFUSS DYSTROPHY: DCM; arrhythmias (AF; Flutter; atrial asystole with junctional rhythm; VT; VF); conduction disorders (including dystrophy secondary to **lamin A/C** mutation)

LIMB-GIRDLE MUSCULAR DYSTROPHY: DCM; prominent R wave in V1; blocks

OTHER NEUROLOGICAL DISEASES

FRIEDREICH'S ATAXIA: autosomal recessive; **concentric HCM** (sometimes localized in the septum); LVOT obstruction; diffuse T wave inversion; possible progression to DCM

MITOCHONDRIAL DISEASES: HCM; DCM; blocks (Kearns-Sayre syndrome); preexcitation

DESMIN-RELATED MYOPATHY: autosomal dominant; conduction disorders; DCM; RCM

GUILLAIN-BARRÉ SYNDROME: HTN; OH; sinus tachycardia; ST abnormalities; tachyarrhythmias / bradyarrhythmias; asystole

MYASTHENIA GRAVIS: myocarditis; arrhythmias; blocks

ACUTE CEREBROVASCULAR DISEASE: ST elevation or depression; T wave inversion; Q waves; ➤ QT (with peaked T wave); neurogenic stunned myocardium; Takotsubo cardiomyopathy; systolic dysfunction; acute pulmonary edema; VT - VF; Torsade de pointes; bradyarrhythmias

CHRONIC RENAL DISEASE

INDEPENDENT CARDIOVASCULAR RISK FACTOR

Accelerated and aggressive CAD; cardiomyopathy; LVH; HTN; valvular heart disease (Ao sclerosis; MAC); vascular calcifications; toxicity of cardiovascular drugs; dyslipidemia (↘ HDL; ➤ TG - ➤ LDL); cardiorenal syndrome; arrhythmias; blocks; infective endocarditis; anemia associated with heart failure; risk of contrast nephropathy; inflammatory state

- To convert serum creatine level mg/dL to mmol/L, multiply by 88.4
- **High output heart failure (AV fistula):** Nicoladoni - Branham sign → ↘ cardiac output (↘ LVOT VTI) after manual compression of the fistula; predictive improved cardiac output after fistula ligation

9.12/ CARDIOVASCULAR COMPLICATIONS OF TRAUMA

PENETRATING INJURY: knife; bullet

- Tamponade; Ischemia (coronary trauma); Complex lesion (valves; coronary arteries; intracardiac fistula)

NONPENETRATING INJURY: compression or deceleration or contusion; safety belt; airbag; steering wheel; fall; collision; rib fractures; CPR

- Contusion; systolic dysfunction; LV free wall rupture (tamponade or hemothorax); RA rupture; ventricular septal rupture; ruptured chordae tendineae or papillary muscle; ruptured valve leaflet (Ao > M > T); Ao rupture; rupture of pericardium (cardiac hernia); arrhythmias; blocks; myocardial infarction (thrombosis; dissection; coronary laceration); *commotio cordis*

SEVERE BURN: toxic myocardial depression for several days (in addition to significant hypovolemia)

ELECTROCUTION: cardiac arrest (VF; asystole); myocardial necrosis; ischemia; arrhythmias; conduction disorder; ECG abnormalities; dysautonomia

MANAGEMENT

ABC; ACLS; Cardiac monitor; NS Bolus; Transfusion; Ultrasound (FAST); OR - Urgent left anterolateral thoracotomy in the case of structural damage

9.13/ POISONING

COCAINE POISONING

SYMPATHOMIMETIC AGENT: inhibition of presynaptic reuptake of norepinephrine and dopamine

CARDIOVASCULAR COMPLICATIONS: sympathetic stimulation; HTN; LVH; ischemia; MI; DCM (excess catecholamines); myocarditis; heart failure (systolic and/or diastolic); arrhythmia; sudden death; endocarditis; aortic dissection; stroke - intracranial hemorrhage; Takotsubo; Brugada pattern on ECG; \uparrow QT (effect on sodium and potassium channels)

MYOCARDIAL INFARCTION: \uparrow O_2 demand; vasospasm; accelerated CAD; thrombosis (\uparrow platelet activation / aggregation); \uparrow plaque rupture; coronary dissection

- > Treatment of myocardial infarction:** O_2 ; ASA; Benzodiazepines; Nitrates; CCB (Diltiazem 20 mg IV); Coronary angiography if persistent ST elevation (thrombolysis if coronary angiography not available and in the absence of contraindication); avoid BB (unopposed alpha-adrenergic stimulation)

BETA-BLOCKER POISONING

PRESENTATION: Symptoms often appear within first 6 h after ingestion: bradycardia; hypotension; cardiogenic shock; altered LOC; seizures; hypoglycemia; bronchospasm

ASSESSMENT: ECG; Glucose; Electrolytes; Ca^{2+} ; BUN; Creatinine; Acetaminophen - Salicylate; beta-HCG

- > ECG:** sinus bradycardia; \uparrow PR interval; \uparrow QRS interval (Propranolol or Acebutolol); bradyarrhythmia; asystole

MANAGEMENT: ABC; Monitor; Atropine (0.5-1 mg IV every 3-5 min up to 0.04 mg/kg); Bolus NS; IV Dextrose; Benzodiazepine if seizures; Activated charcoal (50 g) if patient presents 1-2 h postingestion; Poison Center

IF NECESSARY (IN THE FOLLOWING ORDER)

- a) **Glucagon:** IV bolus 5 mg over 1 min (\pm 2nd bolus in 10 min); if improvement \rightarrow start infusion (2-5 mg/h); target MAP 60 mmHg; Antinausea treatment (Ondansetron)
- b) **IV Calcium:** Calcium chloride (1 g of 10% solution = 10 mL via central line up to a dose of 3 g if necessary) or Calcium gluconate (30 mL of a 10% solution via a central or peripheral line); Monitoring of serum calcium
- c) **Vasopressors:** Epinephrine (1-10 μ g/min; titrate to achieve MAP of 60 mmHg)
- d) **High-dose insulin / Glucose (D5-10%) infusion;** \gg CCB poisoning; K^+ - Mg^{2+} supplement PRN
- e) **IV fat emulsion** (parenteral nutrition)
- f) **Sodium bicarbonate** (1-2 mEq/kg IV \pm infusion) if \uparrow QRS interval
- g) **Endovenous pacemaker:** frequent capture failure; only slight hemodynamic improvement; consider if failure of drug treatment
- h) **IABP / Ventricular assist device** if failure of drug treatment
- i) **Consider hemodialysis** if failure of drug treatment (Atenolol; Nadolol; Sotalol; Acebutolol)

CALCIUM CHANNEL BLOCKER POISONING

DIHYDROPYRIDINE CCB: arterial vasodilatation; reflex tachycardia; effects of nondihydropyridine CCB with high-dose ingestion

NONDIHYDROPYRIDINE CCB: peripheral vasodilatation; bradycardia; negative inotropic agent

ASSESSMENT: ECG; Glucose; Electrolytes; Ca^{2+} ; BUN; Creatinine; Acetaminophen - Salicylate; beta-HCG

MANAGEMENT: ABC; Monitor; Bolus NS; Atropine (0.5-1 mg IV every 2-3 min up to 3 mg); activated charcoal (50 g) if patient presents in 1-2 h post-ingestion; Poison Center

IV CALCIUM: Calcium chloride (10-20 mL of solution 10% x 10 min via central line; repeat up to 4 x if necessary every 20 min) or Calcium gluconate (30 to 60 mL of a 10% solution via a central or peripheral line); Monitoring of serum calcium

- **Infusion:** Calcium chloride (0.2-0.4 mL/kg/h of a 10% solution) or Calcium gluconate (0.6-1.2 mL/kg/h of a 10% solution) if necessary; serum ionized calcium assay every 2 hours; ECG monitoring

IF NECESSARY (IN THE FOLLOWING ORDER)

- a) **Glucagon:** IV bolus 5 mg over 1 min (\pm 2nd and 3rd boluses every 10 min); if improvement
→ start infusion (2-15 mg/h); target MAP 60 mmHg; Antinausea treatment (Ondansetron)
- b) **High-dose insulin / Glucose infusion;** 50 mL D50% if blood glucose < 8.25 mmol/L; Correct potassium
 - **Bolus:** 1 unit/kg of regular insulin IV
 - **Infusion:** 0.5 U/kg/h IV (titrate up to 2 U/kg/h according to response; increase by 0.5 U/kg/h every 20 min)
 - **D5-10% infusion:** 0.5-1 g/kg/h of dextrose; additional bolus of D50% PRN (capillary blood glucose every 15-30 min)
 - **Serum potassium** assay every 30 min (\pm Mg^{2+}); supplement as necessary
- c) **IV vasopressor:** IV Norepinephrine
- d) **IV fat emulsion (parenteral nutrition):** bolus 1-1.5 mL/kg x 1 min (20% solution); Infusion 0.25-0.5 mL/kg/min (30-60 min)
- e) **Other measures:** Endovenous pacemaker (but does not improve contractility); IABP - Ventricular assist device

DIGOXIN POISONING

EXTRACARDIAC MANIFESTATIONS: visual disorders; GI symptoms (nausea; vomiting); neurological symptoms (confusion; muscle weakness); hyperkalemia

CARDIAC MANIFESTATIONS: sinus bradycardia; sinus arrest; ectopic atrial tachycardia with AV block; "regularized" AF (junctional escape rhythm); junctional tachycardia; AV block; PVCs; ventricular bigeminy; VT; bidirectional VT; VF

- **Mechanisms:** **A)** ➤ **Delayed after-depolarizations** (due to ➤ intracellular Ca^{2+}); **B)** ➤ **Automaticity;** **C)** ➤ Vagal tone; **D)** Associated hyperkalemia
- **Digoxin impregnation:** flattening / inversion of T waves; ➤ QT; "scooped" ST segment; ST depression (lateral leads); U waves

ASSESSMENT: Plasma digoxin (6 h post-ingestion if acute poisoning); electrolytes; K^{+} ; Mg^{2+} ; Creatinine - BUN; ECG; Blood glucose

MANAGEMENT: ABC; Cardiac monitoring; Poison Center; Atropine 0.5 mg IV; Bolus NS; Activated charcoal if poisoning < 1-2 h

CORRECT HYPOKALEMIA: as hypokalemia exacerbates the toxic effects; correct hypomagnesemia associated with hypokalemia +

> **Do not correct hyperkalemia**, which is corrected by Digibind

ANTIDOTE: Digibind (anti-Digoxin antibody)

> **Indications: A)** Threatening arrhythmia (symptomatic bradycardia; AV block; ventricular arrhythmia; asystole); **B)** Target organ damage (ARF; altered state of consciousness);

C) Hyperkalemia ($> 5 - 5.5$ mmol/L)

> **1 vial of Digibind neutralizes 0.5 mg of Digoxin** +

EMPIRICAL TREATMENT (ACUTE POISONING WITH UNKNOWN DOSE)	ACUTE POISONING WITH KNOWN INGESTED DOSE	CHRONIC POISONING WITH KNOWN PLASMA DIGOXIN
10 vials (repeat in 30 min if insufficient)	Number of vials = [Ingested dose of Digoxin (mg) x 0.8] / 0.5	Number of vials = [Serum concentration (ng/mL) x patient's weight (kg)] / 100

MAINTAIN ON MONITOR > 72 H if concomitant renal failure (delayed elimination)

HEMODIALYSIS: not indicated

9.14/ SWAN-GANZ CATHETER PLACEMENT

INDICATIONS: A) Cardiogenic shock; **B)** Mixed shock; **C)** Mechanical complication of myocardial infarction; **D)** PHT; **E)** Pretransplantation assessment

1) VERIFICATIONS: patency of ports; test balloon and pressure transducer

2) CENTRAL VENOUS ACCESS: insert the introducer (Cordis) under ultrasound guidance into the internal jugular vein (modified Seldinger technique)

3) SWAN-GANZ CATHETER PLACEMENT: insert the Swan-Ganz catheter by following the natural curvature towards the PA

> Inflate the balloon in the RA (RA hemodynamic curve); keep the balloon inflated while advancing the Swan-Ganz (deflate the balloon on withdrawal)

> Advance the Swan-Ganz while examining changes in the appearance of the hemodynamic curve displayed on the monitor (RA → RV → PA → Wedge)

RA	RV	PA
15-20 cm	30 cm	40 cm

> Withdraw the Swan-Ganz if **< 1 mL of NS** is necessary to inflate the balloon and obtain a Wedge pressure (the catheter tip is probably too distal)

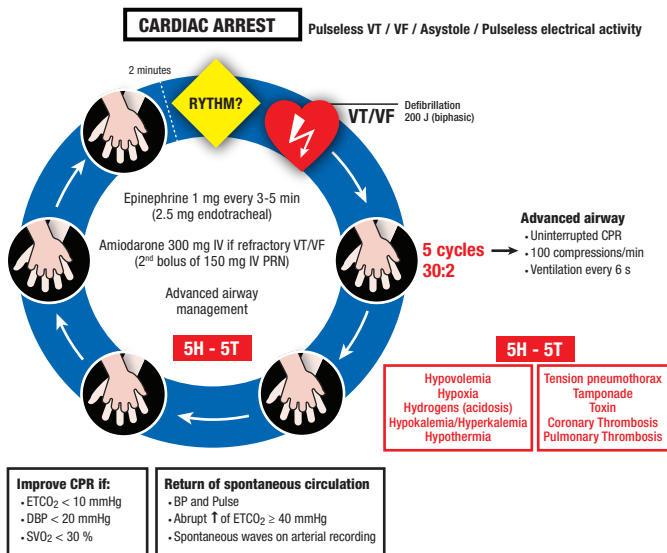
4) CXR: catheter tip < 5 cm from the midline; West zone # 3 preferable

CONSIDER FLUOROSCOPY if chamber dilatation or significant TR

AIR EMBOLISM: left lateral decubitus position (to prevent RVOT obstruction); 100% O₂

9.15/ CARDIOPULMONARY RESUSCITATION

CARDIOPULMONARY ARREST



RECOGNIZE CARDIOPULMONARY ARREST: unresponsive / breathing / pulse

➤ **Activate the survival chain:** 911 - Blue Code - Defibrillator / AED

CARDIOPULMONARY RESUSCITATION

➤ **Cycles: 30 compressions : 2 ventilations**

➤ **Compressions:** lower half of the sternum; 100-120 compressions / min; 5 cm deep (avoid > 6 cm); complete chest recoil between each compression; minimize interruptions

➤ **Ventilation:** Head tilt / Chin lift ("Jaw thrust" if cervical trauma); avoid excessive ventilation

DEFIBRILLATION: Pulseless VT or VF; perform as rapidly as possible

AIRWAY MANAGEMENT

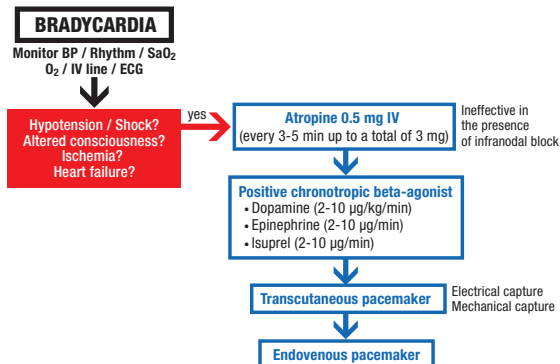
➤ **Initial ventilation:** Ambu mask; 1 s; elevation of the rib cage; avoid excessive ventilation

➤ **Advanced airways support:** allows better ventilation and protects the airways; Endotracheal tube or Laryngeal mask or Combitube

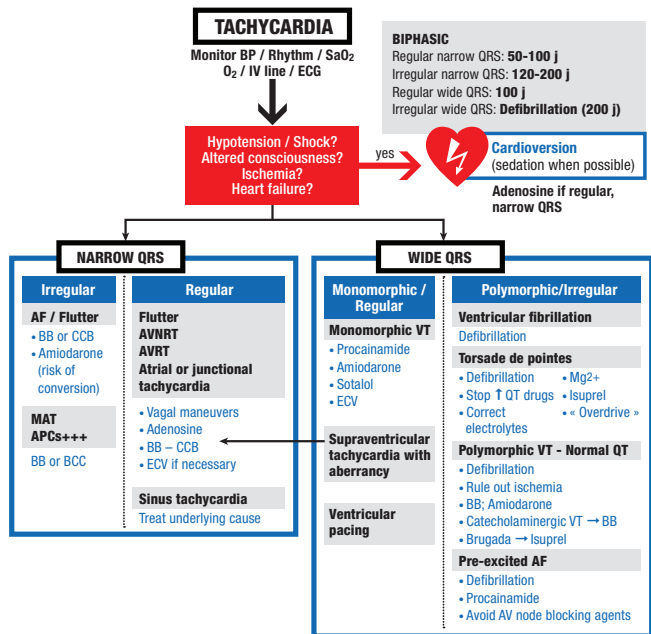
• **Confirmation of position:** **A)** Physical examination (expansion of rib cage; auscultation); **B)** Capnography / CO₂ detector; **C)** Esophageal detector (syringe); **D)** CXR (distal extremity of ETT > 3 cm from the carina)

• **CPR cycles:** Continuous compressions at 100 bpm; Asynchronous ventilation every 6 sec

BRADYCARDIA



TACHYCARDIA



DRUGS USED IN CARDIOPULMONARY RESUSCITATION

Adenosine	<ul style="list-style-type: none"> • 6 mg IV (push) then 20 mL NS • 2nd bolus 12 mg IV PRN 	<ul style="list-style-type: none"> • Supraventricular tachycardia 	Bronchospasm; Hypotension; Flushing; Retrosternal chest pain; Can trigger AF
Amiodarone	<ul style="list-style-type: none"> • 150 mg IV x 10 min (repeat PRN) • Infusion: 1 mg/min x 6 h then 0.5 mg/min (dilution: 450 mg / 250 mL D5%) • Max: 2.2 g / 24 h 	<ul style="list-style-type: none"> • Supraventricular tachycardia • Stable monomorphic VT • Polymorphic VT with normal QT 	Bradycardia; ↑ QT; Long-term toxicity
Beta-blockers	<ul style="list-style-type: none"> • Esmolol: 0.5 mg/kg x 1 min then infusion of 0.05-0.3 mg/kg/min (dilution: 2500 mg / 250 mL) • Metoprolol: 5 mg IV x 1 min (repeat every 5 min up to a total of 15 mg) 	<ul style="list-style-type: none"> • Supraventricular tachycardia • Polymorphic VT associated with ischemia or LQTS or catecholaminergic VT 	Hypotension; Bradycardia; Negative inotrope; Bronchospasm
Diltiazem	<ul style="list-style-type: none"> • 15-20 mg IV x 2 min • 2nd bolus (in 15 min): 20-25 mg IV • Infusion: 5-15 mg/h IV • Dilution: 125 mg/100 mL D5 % (= 1 mg/mL) 	<ul style="list-style-type: none"> • Supraventricular tachycardia 	Hypotension; Bradycardia; Negative inotrope
Lidocaine	<ul style="list-style-type: none"> • Bolus: 1-1.5 mg/kg IV • Perfusion: 1-4 mg/min (30-50 µg/kg/min) • Dilution: 2 g / 500 mL D5% 	<ul style="list-style-type: none"> • Stable monomorphic VT 	Altered state of consciousness; Seizures; Bradycardia
Procainamide	<ul style="list-style-type: none"> • 20-50 mg/min (until suppression of arrhythmia or hypotension or ↑ QRS > 50% or total dose 17 mg/kg) • Dilution: 1000 mg / 250 mL NS 	<ul style="list-style-type: none"> • Pre-excited AF • Stable monomorphic VT 	Bradycardia; Hypotension; ↑ QT; Torsade de pointes; Avoid in the presence of heart failure
Sotalol	<ul style="list-style-type: none"> • 1.5 mg/kg IV x 5 min 	<ul style="list-style-type: none"> • Stable monomorphic VT 	Bradycardia; Hypotension; ↑ QT; Torsade de pointes; Avoid in the presence of heart failure
Magnesium sulfate	<ul style="list-style-type: none"> • 1-2 g IV x 15 min 	<ul style="list-style-type: none"> • Polymorphic VT with ↑ QT 	Hypotension; Respiratory depression
Epinephrine	<ul style="list-style-type: none"> • Dose: 0.1-0.5 µg/kg/min • Dilution: 5 mg / 250 mL D5% 		

Dobutamine	<ul style="list-style-type: none"> • Dose: 2-20 µg/kg/min • Dilution: 250 mg / 100 mL D5%
Dopamine	<ul style="list-style-type: none"> • Dose: 1-20 µg/kg/min • Dilution: 400 mg / 250 mL D5%
Isuprel	<ul style="list-style-type: none"> • Dose: 0.5-10 µg/min • Dilution: 1 mg / 250 mL D5%
Milrinone	<ul style="list-style-type: none"> • Bolus: 50 µg/kg x 10 min • Dose: 0.375 to 0.75 µg/kg/min • Dilution: 10 mg / 100 mL D5% (= 0.09 mg/mL) or 20 mg / 100 mL D5% (= 0.17 mg/mL)
Norepinephrine	<ul style="list-style-type: none"> • Dose: 0.1-0.5 µg/kg/min • Dilution: 4 mg / 250 mL D5% (double PRN)
Phenylephrine	<ul style="list-style-type: none"> • Dose: 0.5-2 µg/kg/min • Dilution: 10 mg / 250 mL NS

MANAGEMENT POST-CARDIAC ARREST

Look for and treat the cause of the cardiac arrest; Coronary angiography if necessary

VENTILATION: Tidal volume 6-8 mL/kg; $\text{SaO}_2 \geq 94\%$; PaCO_2 40-45 mmHg

TARGET ORGAN PERFUSION: NaCl bolus; vasopressors (Epinephrine; Dopamine; Norepinephrine); treat any reversible causes; IABP - Ventricular assist device

- Stunned myocardium x 24-48 h and transient SIRS post-cardiac arrest
- **Targets:** SBP ≥ 90 mmHg; MAP ≥ 65 mmHg; $\text{SVO}_2 \geq 70\%$

TARGETED TEMPERATURE MANAGEMENT

- **Indications:** Comatose adult patients (no meaningful response to verbal commands) with return of spontaneous circulation after cardiac arrest
- **Benefits:** improvement of survival and neurological prognosis (★ Hypothermia after cardiac arrest study group)
- **Targets:** uncertain (between 32°C to 36°C for at least 24 h); intensive treatment of hyperthermia; ★ TTM → no demonstrated benefit of 33°C versus 36°C
- **Complications:** coagulopathy; arrhythmias; ↗ QT; bradycardias; hyperglycemia; infectious risk; hypokalemia / hypomagnesemia / hypophosphatemia

NEUROLOGICAL ASSESSMENT: neurological examination; EEG (rule out seizures in the presence of persistent coma); Brain CT / MRI

- **Factors of poor prognosis (valid after > 72 h):** **A)** Bilaterally absent pupillary light reflex; bilaterally absent corneal reflexes; **B)** Status myoclonus (during the first 72 hours); **C)** EEG with persistent absence of reactivity to external stimuli or with persistent burst suppression or with intractable status epilepticus; **D)** Somatosensory evoked potentials (bilateral absence of cortical response to median nerve stimulation); **E)** Imaging (extensive cortical / subcortical lesions; extensive brain edema)
- **Brain death:** consider organ donation

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Abbreviations

A

AAD: Antiarrhythmic drug
AAA: Abdominal aortic aneurysm
ABC: Airway, Breathing, Circulation
ABI: Ankle-Brachial Index
A/C: Anticoagulant / Anticoagulation
ACEI: Angiotensin-converting enzyme inhibitor
ACLS: Advanced Cardiac Life Support
ACS: Acute coronary syndrome
AF: Atrial fibrillation
AIVR: Accelerated idioventricular rhythm
ALT: Alanine aminotransferase
AML: Anterior mitral leaflet
ANA: Antinuclear antibody
Ao: Aorta
APC: Atrial premature complex
Apo: Apolipoprotein
aPTT: Activated partial thromboplastin time
AR: Aortic regurgitation
ARB: Angiotensin receptor blocker
ARDS: Adult respiratory distress syndrome
ARF: Acute renal failure
ARVD: Arrhythmogenic right ventricular dysplasia
AS: Aortic stenosis
ASA: Acetylsalicylic acid
ASD: Atrial septal defect
AST: Aspartate aminotransferase
ATL: Anterior tricuspid leaflet
AV: Atrioventricular
AVM: Arteriovenous malformation
AVNRT: Atrioventricular nodal reentrant tachycardia

AVR: Aortic valve replacement
AVRT: Atrioventricular reentry tachycardia

B

BB: Beta-blockers
BID: Twice daily
BMI: Body mass index
BMS: Bare metal stent
BNP: Natriuretic peptide type B
BOOP: Bronchiolitis obliterans organizing pneumonia
BP: Blood pressure
BSA: Body surface area
BUN: Blood urea nitrogen
BVR: Balloon Valvuloplasty Registry

C

CABG: Coronary artery bypass graft
CAD: Coronary artery disease
CBC: Complete blood count
CCB: Calcium channel blockers
CCS: Canadian Cardiology Society
CCV: Chemical cardioversion
CK: Creatinine kinase
CM: Cardiomyopathy
CML: Chronic myeloid leukemia
CNS: Central nervous system
CO: Cardiac output
CoA: Coarctation of the aorta
CoNS: Coagulase-negative Staphylococcus
COPD: Chronic obstructive pulmonary disease
COX-1: Cyclooxygenase-1
CPB: Cardiopulmonary bypass
CRF: Chronic renal failure
CRP: C-reactive protein

CRT: Cardiac resynchronization therapy
CS: Coronary sinus
CSNRT: Corrected Sinus Node Recovery Time
CT: Computed tomography
cTn: Cardiac troponin
cTnT HS: Highly sensitive cardiac troponin T
cTnT: Cardiac troponin T
CTO: Chronic total occlusion
CVP: Central venous pressure
CXR: Chest x-ray

D

DBP: Diastolic blood pressure
DCM: Dilated cardiomyopathy
DDx: Differential diagnosis
DES: Drug-eluting stent
DIC: Disseminated intravascular coagulation
DM: Diabetes
dP/dt: Rate of LV pressure rise in early systole
DTS: Duke Treadmill score
DVT: Deep vein thrombosis

E

ECG: Electrocardiogram
ECMO: Extracorporeal membrane oxygenation
ECV: Electrical cardioversion
EEG: Electroencephalogram
EOA: Effective orifice area
EPO: Erythropoietin
EPS: Electrophysiological study
ESR: Erythrocyte sedimentation rate
EVAR: Endovascular aortic repair

F

FAC: Fractional Area Change

FFP: Fresh frozen plasma
FFR: Fractional flow reserve
FMD: Fibromuscular dysplasia

G

GERD: Gastroesophageal reflux disease
GFR: Glomerular filtration rate
GI: Gastrointestinal

H

HbA1c: Glycosylated hemoglobin
HCM: Hypertrophic cardiomyopathy
HDCT: High-definition computed tomography
HDL: High-density lipoprotein
HELLP: HELLP syndrome
HIT: Heparin-induced thrombocytopenia
HR: Heart rate
HSM: Hepatosplenomegaly
HTN: Hypertension

I

IABP: Intra-aortic balloon pump
IART: Intraatrial reentry tachycardia
ICD: Implantable cardioverter-defibrillator
IDU: Intravenous drug user
IMT: Intima-media thickness
INR: International normalized ratio
ISA: Intrinsic sympathetic activity
IUGR: Intrauterine growth retardation
IVC: Inferior vena cava
IVCT: Isovolumic contraction time

IVRT: Isovolumic relaxation time
IVS: Interventricular septum
IVUS: Intravascular ultrasound

J

JVD: Jugular vein distension

L

LA: Left atrium
LAA: Left atrial appendage
LAD: Left anterior descending
LAH: Left atrial hypertrophy
LAHB: Left anterior hemiblock
LAO: Left anterior oblique
LBBS: Left bundle branch block
LMCA: Left main coronary artery
LDH: Lactate dehydrogenase
LDL: Low-density lipoprotein
LFTs: Liver function tests
LGE: Late gadolinium enhancement
LIMA: Left internal mammary artery
LMWH: Low molecular weight heparin
LPHB: left posterior hemiblock
LPL: Lipoprotein lipase
LQTS: Long QT syndrome
LV: Left ventricle
LVAD: Left ventricular assist device
LVDD: Left ventricular diastolic diameter
LVEDP: Left ventricular end-diastolic pressure
LVEF: Left ventricular ejection fraction
LVH: Left ventricular hypertrophy

LVOT: Left ventricular outflow tract
LVSD: Left ventricular systolic diameter

M

M: Mitral
MAC: Mitral annular calcification
MAO inhibitor: Monoamine oxidase inhibitor
MAP: Mean arterial pressure
MCP: Metacarpophalangeal
MET: Metabolic Equivalent of Task
MIBIP: MIBI-Dipyridamole
MPA: Main pulmonary artery
MR: Mitral regurgitation
MS: Mitral stenosis
MSK: Musculoskeletal
MTX: Methotrexate
MVP: Mitral valve prolapse
MVR: Mitral valve replacement

N

NGT: Nasogastric tube
NIHSS: NIH Stroke Scale
NNT: Number needed to treat
NPO: Nil per os
NPV: Negative predictive value
NSAID: Non-steroidal anti-inflammatory drug
NSVT: Non-Sustained Ventricular Tachycardia
NYHA: New York Heart Association

O

OH: Orthostatic hypotension
OR: Operating room
OSAHS: Obstructive sleep apnea / hypopnea syndrome
OTP: Orthopnea

P

PA: Pulmonary artery
PAD: Peripheral artery disease
PAH: Pulmonary arterial hypertension
PAN: Polyarteritis nodosa
PAP: Pulmonary artery pressure
PAT: Paroxysmal atrial tachycardia
PCI: Percutaneous coronary intervention
PCR: Polymerase chain reaction
PDE-5: Phosphodiesterase-5
PET: Positron emission tomography
PET-FDG: Fluorodeoxy-glucose positron emission tomography
PFO: Patent foramen ovale
PFTs: Pulmonary function tests
PHT: Pressure half time
PHT: Pulmonary hypertension
PISA: Proximal isovolumic surface area
PDA: Posterior interventricular artery
PJRT: Paroxysmal junctional reentry tachycardia
PLAX: Parasternal long axis
PML: Posterior mitral leaflet
PMR: Polymyalgia rheumatica
PMT: Pacemaker-mediated tachycardia
PNC: Penicillin
PND: Paroxysmal nocturnal dyspnea
PO: Per os
POTS: Postural orthostatic tachycardia syndrome
PPD: Purified Protein Derivative (Mantoux test)

PPI: Proton pump inhibitor
PPM: Permanent pacemaker
PPV: Positive predictive value
PR: Pulmonary regurgitation
PRN: As needed
PS: Pulmonary stenosis
PSAX: Parasternal short axis
PSVT: Paroxysmal Isupraventricular tachycardia
PT: Prothrombin time
PTCA: Percutaneous coronary angioplasty
PTL: Posterior tricuspid leaflet
PTU: Propylthiouracil
PV: Pulmonary vein
PVAB: Post-ventricular atrial blanking
PVARP: Post-ventricular atrial refractory period
PVE: Prosthetic valve endocarditis
PVR: Pulmonary valve replacement
PVR: Pulmonary vascular resistance

Q

QD: Once daily
QID: Four times a day

R

RA: Rheumatoid arthritis
RA: Right atrium
RAA: Right atrial appendage
RAH: Right atrial hypertrophy
RAO: Right anterior oblique
RBBB: Right bundle branch block
RCA: Right coronary artery
RCM: Restrictive cardiomyopathy
RCT: Randomized controlled trial
RF: Radiofrequency

RF: Rheumatoid factor
RF: Risk factor
RPA: Right pulmonary artery
RUQ: Right upper quadrant
RV: Right ventricle
RVAD: Right ventricular assist device
RVG: Radionuclide ventriculography
RVH: Right ventricular hypertrophy
RVOT: Right ventricular outflow tract
RVSP: Right ventricular systolic pressure
RWMA: Regional wall motion abnormality
RWT: Relative wall thickness

S

SA: Sinoatrial
SAECG: Signal-averaged ECG
SAH: Subarachnoid hemorrhage
SAM: Systolic anterior movement of mitral leaflet
SaO₂: Oxygen saturation
SBP: Systolic blood pressure
SIRS: Systemic inflammatory response syndrome
SLE: Systemic lupus erythematosus
SPEP: Serum protein electrophoresis
SQTS: Short QT syndrome
SR: Sinus rhythm
SSRI: Selective serotonin reuptake inhibitor
SSS: Sick sinus syndrome
STS: Society of Thoracic Surgeons
STEMI: ST segment elevation myocardial infarction
STL: Septal tricuspid leaflet
SVC: Superior vena cava

SVO₂: Venous oxygen saturation

SVR: Systemic vascular resistance

T

T: Tricuspid

TARP: Total atrial refractory period

TAVI: Transcatheter aortic valve implantation

TB: Tuberculosis

TEE: Transesophageal echocardiography

TG: Triglycerides

TGV: Transposition of the great arteries

TIA: Transient ischemic attack

TID: Three times a day

TNK: Tenecteplase

TNT: Nitroglycerin

TOF: Tetralogy of Fallot

TR: Tricuspid regurgitation

TTE: Transthoracic echocardiography

TTR: Transthyretin

TVR: Tricuspid valve replacement

TXA-2: Thromboxane-2

U

ULN: Upper limit of normal

URI: Upper rate interval

URTI: Upper respiratory tract infection

US: Ultrasound

V

VAC: Vacuum assisted closure

VF: Ventricular fibrillation

VLDL: Very low density lipoprotein

VO₂: Oxygen consumption

VPC: Ventricular premature complex

VSD: Ventricular septal defect

VT: Ventricular tachycardia

VTI: Velocity-time integral

vW: von Willebrand

W

WMSI: Wall motion score index

WPW: Wolff-Parkinson-White



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